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# GRANULOSAL CELL TUMORS OF THE OVARY*

### A Report of Three Recent Cases

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IN the *Annals of Surgery* of November, 1935, there is a report of "Ovarian Tumors with Endocrine Significance," from the Massachusetts General Hospital.[3] At that time 7 cases of granulosal cell tumors had been found among the ovarian tumors catalogued in the pathology laboratory. The search for these tumors was carried out upon all slides of ovarian tumors for a 10-year period. The recognition of granulosal cell tumors is rather recent, and many surgeons and pathologists have never seen one. That they are not unusually rare is evident from the fact that 3 cases have been operated upon in the past year, 2 at the Massachusetts General Hospital and 1 at the Pondville Hospital. It is the purpose of this paper to describe briefly and as clearly as possible what such a tumor is, how it can be diagnosed, its origin and the different types that are seen.

#### HISTORY

In the textbooks of gynecology and pathology but slight mention has been made of these tumors until recently. Prof. Dr. Robert Meyer of Berlin is responsible in a large measure for the great interest that has been aroused concerning them. Practically all the available information regarding such tumors, including reports of cases, dates from 1930. In this country E. Novak,[5, 6] of Baltimore, S. H. Geist,[1] of New York, R. W. TeLinde,[9] of Baltimore and others have contributed many articles on the subject. In 1928 Graves[2] wrote in his textbook of an ill-defined group of tumors known as folliculomas, oophoromas and granulosal cell tumors. Real knowledge of the lesion, especially knowledge of its endocrine significance, was absolutely lacking. More recently it has been shown by Schuschania[7] that these tumors secrete estrin, the female sex hormone, and they are, therefore, known as feminizing tumors. Meyer has advanced the accepted theory of their origin from granulosal cell rests or the pregranulosal cells that are found in the medulla near the hilum of the ovary.

#### THE TUMOR

A granulosal cell tumor, follicle cell tumor, or oophoroma folliculare is a tumor composed of cells that resemble very closely the cells of the granulosa of the normal graafian follicle. Moreover, like the cells of the follicle, the tumor is capable of secreting the female sex hormone known as estrin, folliculin or theelin. If this tumor can secrete estrin, it must affect the patient in the same manner that continuous estrin production would. It should be possible for estrin to be extracted from the blood and urine of such a patient in quantities that are greater than normal, and estrin should be found in the tumor itself. That this is true will be shown in the laboratory studies done upon 1 of the patients (case 2) described in this paper.

Granulosal cell tumors grow in such various forms as cylindromatous, moiré silk, sarcomatous, tubular and follicular. There are at least three types of the tumor, for just as the corpus luteum is probably composed of luteinized granulosal cells, there is also the possibility of a granulosal cell tumor changing to a luteoma or corpus luteum tumor under certain circumstances. It is known that the theca interna of the graafian follicle secretes estrin, and, inasmuch as this tissue (theca) is closely related to granulosal cells and lutein cells,—there are some who believe that lutein cells are derived, at least in part, from the theca,—a tumor composed of thecal cells must be included in the group of tumors known as granulosal cell tumors. Thus, we have various methods of cell growth and three different types of tumors.

The granulosal cell tumor may be of almost any size from a millimeter to 20 or 30 centimeters in diameter. Nevertheless, the lesion is usually quite uniform, being about the size of a lemon or an orange, and is nearly always unilateral. It is usually a solid tumor with cystic areas in it, and there is a characteristic yellow tinge to the tumor tissue, some areas being more yellow than others.

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ORIGIN

There is considerable controversy as to the origin of these tumors, but most pathologists are now in accord with Meyer and believe that it lies in the indifferent sex cells that are found in the hilum of the ovary. These indifferent cells arise from the inner epithelial cell mass and possibly the outer cell mass that together make up the ovary (fig. 1). Ova, which are later surrounded by granulosal and thecal cells, may arise in the germinal epithelium of the ovary, which arises from the outer cell mass, or from the primitive genital cells of which the inner cell mass is partly composed. It is from the indifferent cells of the inner cell mass that the cells of the granulosa and theca arise, and it is from these that this tumor probably originates. In the diagram of the developing ovary (fig. 1), eggs are shown coming from the germinal epithelium and from the cells of the inner epithelial mass. The cells that surround the eggs are the indifferent cells that are pregranulosal and prethecal. While, as has just been said, the tumors probably arise from these cells, it is logical, when one compares the great similarity of the granulosal cells of the graafian follicle (fig. 2) with the granulosal cells of the tumor, to consider that the tumor may have arisen directly from the former. In the diagram of the normal adult ovary (fig. 2), granulosal cells of the follicle are shown, and it is possible that in some instances tumors arise from these cells.

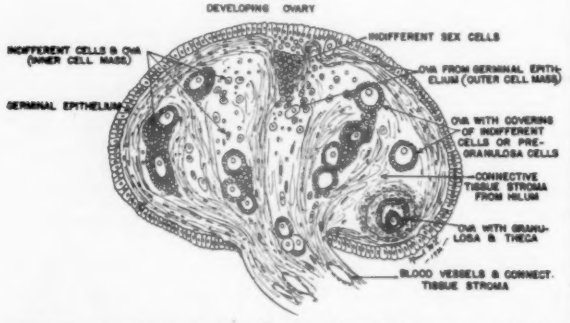
DEVELOPING OVARY
INDIFFERENT SEX CELLS
INDIFFERENT CELLS & OVA (INNER CELL MASS)
OVA FROM GERMINAL EPITHELIUM (OUTER CELL MASS)
GERMINAL EPITHELIUM
OVA WITH COVERING OF INDIFFERENT CELLS OR PRE-GRANULOSA CELLS
CONNECTIVE TISSUE STROMA FROM HILUM
OVA WITH GRANULOSA & THECA
BLOOD VESSELS & CONNECT. TISSUE STROMA

FIG. 1. A schematic drawing of a developing ovary, showing the germinal epithelium (from the outer cell mass) forming ova and indifferent cells. The ova and indifferent cells of the inner cell mass are already present in the medulla of the ovary. These indifferent cells or prethecal or pregranulosal cells become thecal and granulosal cells after they have surrounded an ovum, as is shown in the lower right-hand corner of the drawing. The indifferent cells, or pregranulosal and prethecal cells, are the originating cells for the granulosal cell tumors.

HISTOLOGY

As has already been mentioned, these tumors grow in various forms, but the cells of all of these forms have some resemblance to true granulosal cells. The follicle type is the most characteristic; it is made up of cells that look very much like follicle granulosal cells, and small areas that try to form follicles are occasionally observed. The epithelium palisades itself around some cell debris, and the result simulates very closely the early primordial follicle. In other areas are the so-called Call-Exner bodies or groups of granulosal cells surrounding a small area of cystic liquefaction. The similarity to primordial follicles and ova is striking, and it was formerly thought that these tumors were capable of producing both new follicles and ova. Other tumors grow in tubular fashion, there being clear-cut tubules made up of granulosal cells, and certain others grow in cylindromatous fashion. The moiré silk type is made up of short cords of tumor tissue which are split up by connective tissue septa. The sarcomatous type is not rare, and it is due to this type of growth that many pathologists have considered that these tumors must be related to sarcomas. It is always necessary to look at many microscopic sections before a diagnosis is made, for, although one area may not even suggest such a tumor, another area may be found to be typical. Many sections must be cut, and the diagnosis will be definite only if typical granulosal cells are seen. Unquestionably, in the enthusiasm of the moment, many reports are being made of tumors that are "odd" histologically and that are erroneously considered to be granulosal cell tumors. In most instances the true granulosal cell tumor is easy to diagnose histologically, but there are rare tumors that only long experience will enable one to recognize as being of this type. On gross and histologic examinations, a thecal cell tumor closely resembles a fibroma of the ovary, but some of its cells contain lipoid and the connective tissue is hyaline in type. Thecal cell granulosal cell tumors are accompanied by the typical symptoms and biologic characteristics of the granulosal cell tumor. The

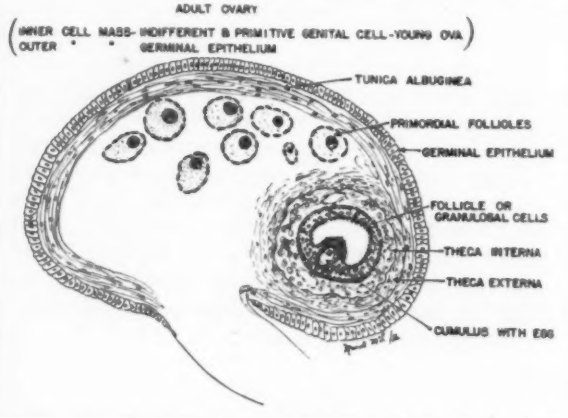


FIG. 2. This shows many primordial follicles and a fully developed graafian follicle. The cells of the graafian follicle are composed of theca externa, theca interna and granulosal cells. The cells of these structures closely resemble the cells of the thecoma and the granulosal cell tumor.

thecoma, or the fibroma-like type of granulosal cell tumor of the ovary, is more common in older women. This may be due to the fact that the granulosal cells are absent from the ovary of the postmenopausal patient, while the thecal cells are still present—an explanation that is based on the presumption that these tumors arise from the adult cells, concerning which there is some question. It is possible, however, that the prethecal cells are more persistent at the menopause than are the pregranulosal cells.

### LABORATORY DATA

All types of granulosal cell tumors secrete estrin, but whether the amount of secretion is continuous, and whether it is large, normal or smaller than normal is not known. It is reported that the thecal cell tumor secretes a greater amount of estrin than does the true granulosal cell tumor. Because of the presence of estrin in the urine, blood, tumor, cyst fluid, uterus, and so forth, it is obvious that certain of the biologic effects of estrin must occur in the patients. In case 2 of this series, Dr. Frederic Parker, Jr., of the Boston City Hospital, carried out studies which showed that the urine contained less than 166 rat units of estrin per liter and less than 166 rat units of prolan per liter; that the uterus contained less than 100 mouse units of estrin per kilogram (wet weight); and that the tumor contained 530 mouse units of estrin per kilogram (wet weight). It was further shown that the mouse injected "remained in complete estrus for 5 or 6 days, which in my experience (Dr. Parker) is longer than usual. The mouse showed beginning estrus 48 hours following injection which, as you know, is unusually early. The mouse was finally autopsied to make sure no ovarian tissue was still present, and none was found." On the other hand, in case 1 of this series no estrin was found in the urine, cyst fluid or tumor when examined in Dr. Albright's laboratory at the Massachusetts General Hospital. This lack of estrin may represent one phase in the biology of these tumors, and the presence of estrin another. The presence of a continuous and increased secretion of estrin should have certain effects on patients, such as periods of amenorrhea followed by flowing, periods of abnormal flowing, growth of breast epithelium, and hyperplasia of the endometrium. It should be responsible for precocious puberty and a return of bleeding after the menopause. It also could cause an inhibition of the pituitary, at least so far as the production of sex hormones is concerned. It should prevent ovulation and, therefore, be a cause of sterility. These effects of estrin production are evident in the symptomatology of patients with these tumors.

### SYMPTOMS AND SIGNS

The presence of such a tumor in young people usually causes precocious genital development owing to an excess of estrin. The patient menstruates early and the periods are irregular and anovulatory. The breasts are well-developed, and other secondary sex characteristics are present early. The endometrium of such a patient shows evidence of proliferation or estrin influence, but no evidence of secretion or of corpus luteum effect. Removal of such a tumor restores normal development. In 1934 Novak[5] described children with such precocious development.

An adult patient with such a tumor usually has periods of amenorrhea (continuous estrin production) before a period of abnormal bleeding of the anovulatory type. Overdevelopment of the breasts is not unusual, and the presence of areas of hyperplasia, either throughout the breast or in discrete areas, with the formation of a tumor nodule, is not surprising. Endometrial biopsy shows an endometrium with the estrin effect of proliferation or hyperplasia, and there should be no evidence of a functional or corpus luteum effect. Removal of such a tumor allows the ovary to function properly—ovulation should take place, and periods of amenorrhea and menorrhagia ought to give place to normal ovulatory periods.

If such a tumor occurs after the menopause, it causes reactivation of the endometrium, which is accompanied by periods of abnormal bleeding or even by periods of rhythmic bleeding. This bleeding is of the anovulatory type and comes from a definitely proliferative type of endometrium. There should be no corpus luteum phase. Women past the menopause who bleed and in whom an estrin or proliferative effect or hyperplasia of the endometrium is found should be carefully studied for the presence of a granulosal cell tumor. In such women the breast may take on some evidence of growth, and the vagina, which ordinarily is pink and atrophied, may become bluish and moist along with a regrowth of normal vaginal epithelium. The symptoms, therefore, are those caused by estrin, with breast, endometrial and vaginal changes.

A recent case at Pondville has attracted our attention. A woman of 84 with abnormal bleeding was found to have a normal, soft, smooth, bluish vagina. On curettage her endometrium showed a real hyperplasia, her urine contained estrin, and, on pelvic examination, a tumor was considered to be present. Although all the signs and symptoms of such a lesion were present, her age and physical condition did not warrant an operation. This case is mentioned to show the extreme age at which this feminizing tumor may be present.

### DIAGNOSIS

Any signs of developmental precocity in a young girl suggest the possible presence of this tumor, although it is not always present, for there are normal girls who mature early. Furthermore, such early maturity may be due to precocious pituitary development and to an ovary that is ovulating too early. Since graafian follicles are developed even before the age of 2, it is not difficult to understand how, with just a little extra push from the pituitary, ovulation might take place, and menstruation follow at an early age. All precocious flowing is abnormal, but it may be merely an evidence of a generalized precocity. If it were possible to do successive endometrial biopsies upon such a patient, the finding of a secretory or corpus luteum phase would rule out the presence of a granulosal cell tumor but would not exclude a luteoma. The latter tumor is so rare, however, that it could be practically excluded. If it should be present in a young girl, it would cause the development of a secretory endometrium. As successive endometrial biopsies cannot be done in young girls, a curettage or endometrial biopsy under anesthesia just before the expected period would tell whether ovulation had taken place. If ovulation had not occurred, the presence of a granulosal cell tumor should be seriously considered. A quantitative study of the estrin in the urine would be of importance, and a high urine estrin, coupled with her precociousness and an estrin phase in the endometrium, ought to establish the diagnosis.

In an adult patient the diagnosis can be made upon a history of abnormal bleeding and the presence of an excess of estrin in the urine, plus five successive weekly biopsies, all of an estrin phase. Metropathia hemorrhagica or Shaw type I bleeding might be confusing, since an estrin endometrium of the Swiss-cheese type is always present because of the persistent follicle cyst and the absence of a corpus luteum in the ovary. However, the presence of a tumor mass, which is larger and firmer than a follicle cyst, plus a high urine estrin and true hyperplasia of the endometrium, should establish the diagnosis.

In older women the occurrence of bleeding after the menopause should make one suspicious, especially if cancer of the body of the uterus can be ruled out, and if the endometrium shows hyperplasia. If the urine contains estrin, the diagnosis ought to be almost certain, for normal women do not have estrin in their urine after the menopause, whereas patients with granulosal cell tumors do. If, coupled with the above findings, a definite softening and bluing of the vagina is found, and if the patient has had any breast discomfort, the diagnosis ought to be fairly clear.

### TREATMENT

Granulosal cell tumors should be operated upon and removed. These lesions are rarely bilateral and are not always malignant. If the patient is a young girl or a young child, it is much wiser to be conservative than to be radical. However, in a woman near the menopause or past the menopause, it is better to be radical and to remove both tubes, both ovaries and the uterus, as if dealing with a malignant ovarian tumor. Occasionally, in younger women and children a recurrence will take place or a tumor develop in the other ovary, but the chances are not great, and it is not necessary to advocate radical surgery in all cases.

### CASE REPORTS

*Case 1* (Massachusetts General Hospital). The first case to be discussed is that of a 32 year old,

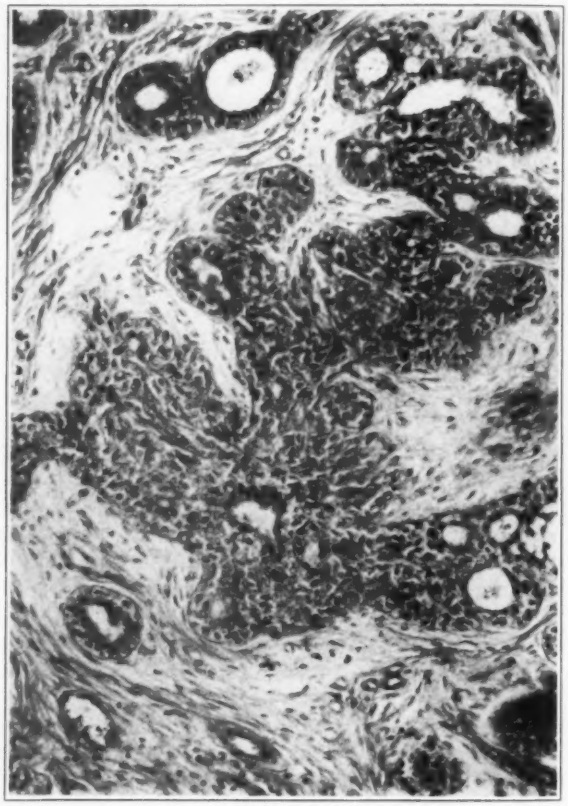

FIG. 3. *Case 1.* Photomicrograph of a breast lesion removed 6 years before the ovarian tumor. This intracanalicular papillary adenofibroma shows marked proliferation of the epithelium. It is considered that the granulosal cell tumor was present at the time this breast lesion was removed.

single woman. In 1929, at the age of 26, she was operated upon at the New England Deaconess Hospital, and a lesion of the breast was removed. The tumor nodule was examined by Dr. Shields Warren, who felt that it was a very early cancer of the breast growing from the epithelium of an intracanalicular papillary adenofibroma, with marked epithelial proliferation. On restudy of this tumor it is obvious that there is far too much proliferation for an ordinary intracanalicular tumor (figs. 3 and

4) and that early cancer may be present.* Its great activity raises the question as to whether a granulosal cell tumor was not the real cause of the marked epithelial overgrowth at that time. Breast tumors are known to accompany these lesions, and because of its odd growth and the marked proliferation, it is fair to assume that the pelvic tumor, though perhaps very small, was probably present at that time. The patient's periods began at the age of 12 and occurred regularly every 28 days with a scanty flow of 2 days' duration.

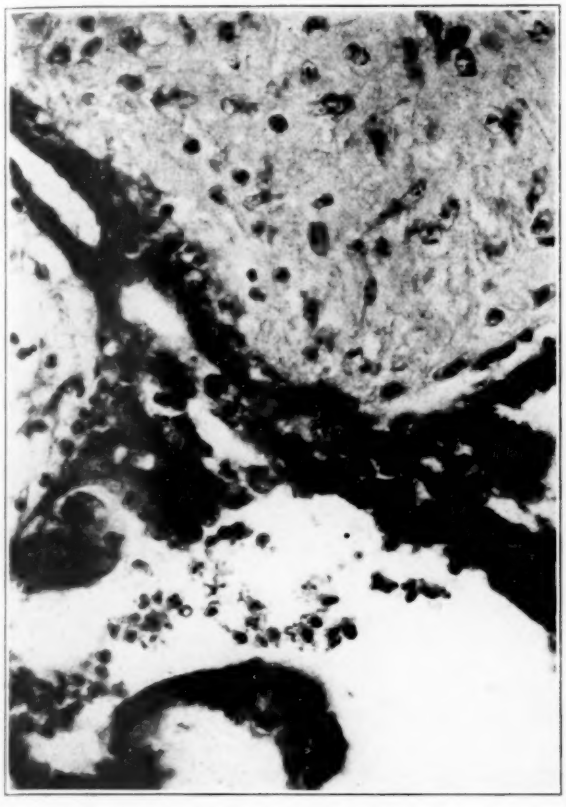

FIG. 4. *Case 1.* High power photomicrograph of an edge of the epithelial proliferation in the breast tumor. Dr. Shields Warren considers that this represents early carcinoma of the breast. See his description in the footnote below.

In February, 1936, she was seen at the Massachusetts General Hospital because of flowing that had been nearly constant for 1 year and 9 months, following a period of amenorrhea that had lasted for 6 months. A dilatation and curettage was done, and the tissue showed definite hyperplasia of the endometrium (fig. 5). At that time no tumor was found in the pelvis. Following this operation, the patient was well for 1 month, after which she began to have bimonthly flowing. Weekly biopsies were started in the Ovarian Dysfunction Clinic, and all biopsies, even those just before and during her period, showed an estrin or proliferative phase. A tumor of the ovary was noted, and she was referred into the hospital with a diagnosis of a granulosal cell tumor. Her urine was examined for estrin and it was found to be present. Her prolan A test was negative.

On May 29, 1936, Dr. H. K. Sowles operated upon the patient and removed a solid tumor of the right ovary 7.5 by 10.0 centimeters in size (fig. 6). The rest of the pelvic organs were normal and were not disturbed. In June she had a small period that lasted for 1 day and in July a large one that lasted for 5 days when the flowing stopped abruptly as in normal menstruation. A biopsy taken 23 days after this period showed an estrin phase in the endometrium, when it should have been in the secretory phase (fig. 7). The exact significance of this cannot be explained.

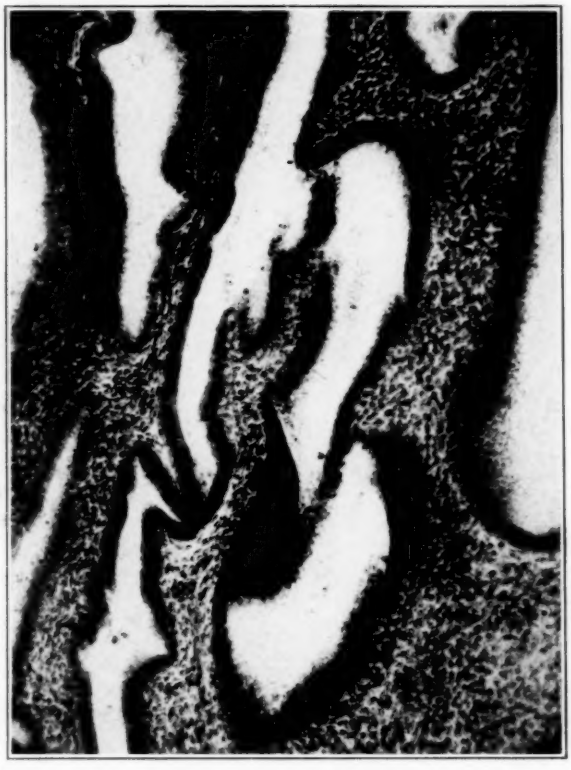

FIG. 5. *Case 1.* Endometrium, which was removed at a curettage 3 months before operation after a year and one half of nearly continuous bleeding, and which shows typical estrin or proliferative phase (hyperplasia) of the endometrium.

Biologic assay of the urine that was collected just after the operation, of the tumor, and of some of the fluid present in small cysts in the tumor failed to give positive estrin readings. This finding confuses our ideas of the biology of these interesting tumors.*

*(Letter from Dr. S. Warren) "Fig. 3 shows a focus of active epithelial proliferation in the adenofibroma. Fig. 4 shows a focus of marked epithelial hyperplasia with loss of basement membrane and invasion of stroma that I think entitles it to a diagnosis of carcinoma. This was at the margin of an intracanalicular adenofibroma. Several mitotic figures can be noted, as well as the epithelial invasion. For those who take any stock in such things, the large size of the nucleoli can be made out."

*The exact methods of assay of the urine, cyst fluid, and tumor in this case are described by Dr. Sulkowich of Dr. Albright's laboratory as follows:

"The total weight of the ovary was 122 gm. A 35 gm. portion of the ovary was taken and digested with sulfuric acid in a buffer mixture containing sodium acetate and sodium hydroxide. The pH was adjusted to between 1 and 2 with thymol blue. The tissue was allowed to dissolve slowly by standing in this mixture and was then boiled for 2 hours. The pH was readjusted to between 1 and 2 with sulfuric acid, and the hydrolized mixture was extracted with isopropyl ether. The isopropyl ether was evaporated, and the estrogenic substances were taken up in olive oil that was assayed in spayed rats for 7, 14 and 28 rat units of estrin. All of the assays were negative for estrin.

"The cyst fluid yield was 0.5 cc. and was assayed by direct injection in spayed rats for 10, 20, 40, and 80 rat units of estrin. All of the assays were negative for estrogenic substances.

"The urine was assayed by adjusting the pH to between 1 and 2 and adding an additional 1 cc. of sulfuric acid, specific gravity 1.84. This was boiled for 2 hours, and two 300 cc. aliquots were extracted with isopropyl ether. The isopropyl ether was concentrated, and estrogenic substances were taken up in olive oil and injected in spayed rats. The total amount of urine for 24 hours on May 4, 1936 was 2,200 cc., and this was found to contain 22 rat units of estrin. The total 24-hour amount on May 30, 1936, was 700 cc. This was assayed for 10 rat units and was negative for estrogenic substances."

The tumor was solid and cystic and contained large areas of yellow tissue so characteristic of the granulosal cell tumor (fig. 6). Microscopically, it was a follicular type of granulosal cell tumor (fig. 8).

FIG. 6. *Case 1.* Drawing of the tumor showing the cystic areas. The white areas in the drawing were yellow in the original specimen, which was a smooth, rounded, solid and cystic tumor about the size of an orange.

This patient had had a definite breast disturbance (excessive proliferation) 6 years before her granulosal cell tumor was found. She had had estrin phase endometria on five successive, weekly biopsies. Because an ovarian tumor was present, plus the reports on the biopsies, plus the report of the breast tumor, a diagnosis of a granulosal cell tumor had been made, which proved to be correct. The chart (fig. 9) shows the periods and the dates of the biopsies and their interpretation before operation was decided upon. In this patient the diagnosis seemed quite probable, and our investigations and knowledge of the history made the interpretation an accurate one.

*Case 2* (Pondville Hospital). The patient, a 38 year old woman with four children, came to the hospital complaining of amenorrhea and a vaginal discharge of 6 months' duration. Twelve years before she had been operated upon, and the right tube and ovary were removed. She had a badly infected cervix with exposure of the endocervix, and on October 29, 1935, one of us (L. P.) did a curettage, amputated her cervix, and repaired her perineum. A tumor nodule was felt in the left vault, and, at a subsequent operation on November 12, 1935, a hysterectomy was performed with removal of the left tube and ovary. The tumor of the left ovary was solid, hard and firm, and was about the size of a lemon. Tissue removed with the curet at the first operation showed a resting endometrium that was without evidence of estrin effect. The tumor of the ovary that was removed at the second operation was seen by Dr. Shields Warren, Dr. Frederic Parker, Jr., Dr. Tracy Mallory, Dr. Howard T. Karsner and the authors, and all agreed that it was a granulosal cell tumor of a rather peculiar type. There was present a polyp of the endometrium. The tissue of the tumor, the uterus and the urine were studied by Dr. Frederic Parker, Jr., at the Boston City Hospital, and his report concerning the estrin in the urine, tumor and uterus has been given above.

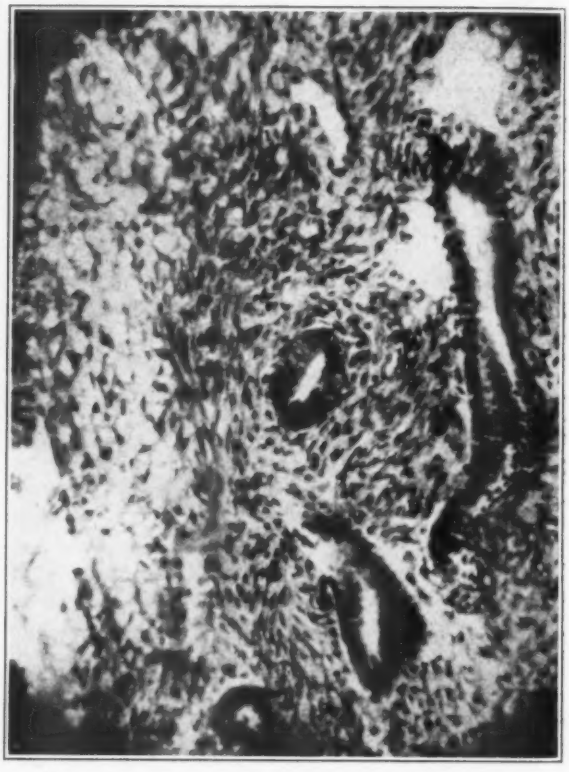

FIG. 7. *Case 1.* A small piece of endometrium from an endometrial biopsy 23 days after the onset of the patient's first menstruation after operation. Here a secretory or corpus luteum phase would be expected, but it is obvious that only the proliferative or estrin phase is present.

This patient had a granulosal cell tumor, and was in the amenorrheic phase that occasionally occurs. The diagnosis of the tumor would not have been possible on the information obtained from the history and endometrial biopsy, but on the removal of the tumor, its appearance, both grossly and histologically, was considered very suggestive, and on subsequent examination it was proved to be of the granulosal cell type. Figure 10 shows the tumor just after its removal—a solid, smooth type of lesion accompanied by an endometrial polyp. The histologic picture is that of an "odd" type of granulosal cell tumor (fig. 11). The polyp can probably be explained on the basis of prolonged estrin influence.

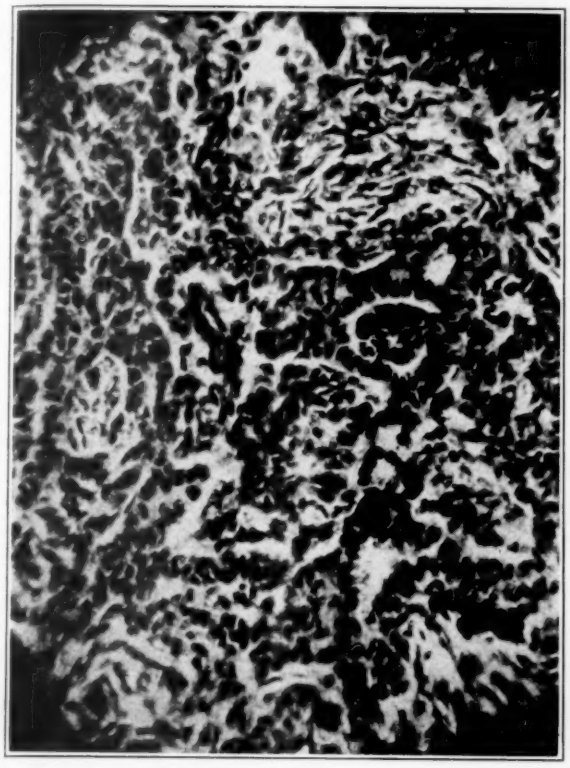

FIG. 8. *Case 1.* This tumor is typical of the common follicular type of granulosal cell tumor. Palisade-like cells can be seen trying to form follicular areas. When one of these groups of cells surrounds epithelial debris or small accumulations of fluid, the so-called Call-Exner body is formed.

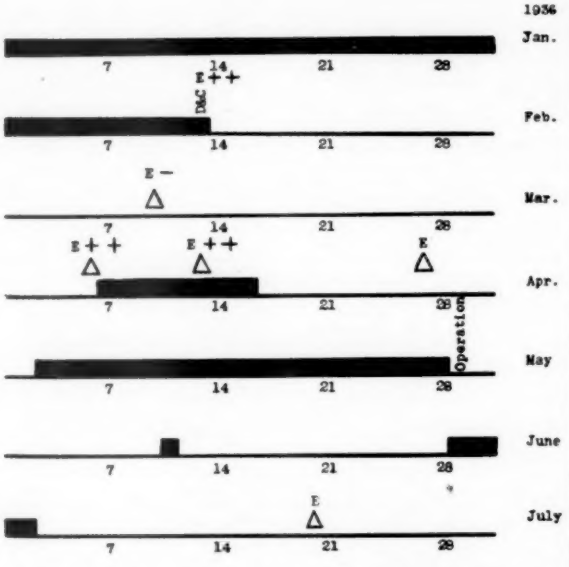


FIG. 9. *Case 1.* This chart shows the periods of the patient from January, 1936, to July, 1936. The heavy areas denote flowing, the small triangles the dates of the endometrial biopsies, and the "E" means estrin phase. This graphically demonstrates when the biopsies were taken with relation to the flow and indicates that at all times during the cycle only estrin phases were present.

FIG. 10. *Case 2.* Photograph of the uterus with the firm, round and glistening tumor. It was about the size of a lemon. Very few cystic areas were present. There was a large endometrial polyp, but no generalized hyperplasia of the endometrium.

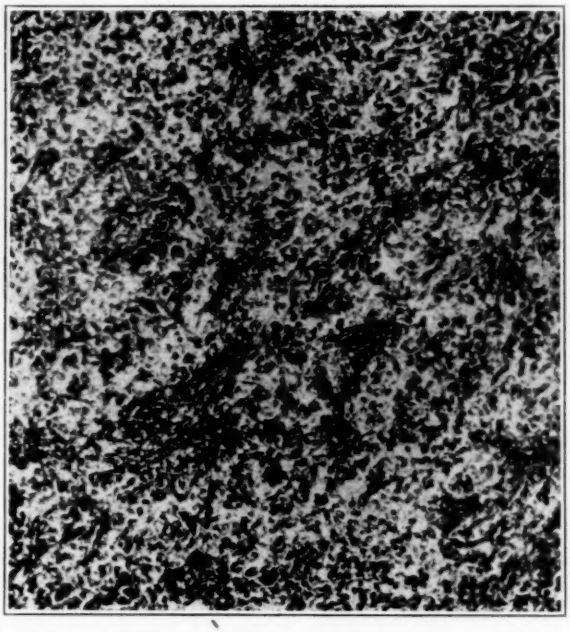

FIG. 11. *Case 2.* Photomicrograph of the tumor shown in figure 10. Here are groups of granulosal cells separated by loosely meshed, connective tissue stroma. Loosely meshed stroma is said to be characteristic of the tumor.

*Case 3* (Massachusetts General Hospital). This patient was a 65 year old widow with one child. She came to the hospital because of menorrhagia of 5 years' duration. Her periods began at 12, were regular every 28 days, and of 4 to 5 days' duration. She had had her menopause 8 years before. Almost every month for the past 5 years she had been flowing in large quantities. On October 10, 1934, a dilatation and curettage were carried out, and radium given. The amount of endometrium removed was so great that at operation one of us (L. P.) felt it must represent a tumor of the endometrium. A diagnosis of hyperplasia of the endometrium was made by the pathologist, and the question of granulosal cell tumor was considered; but because the patient was in poor physical condition, an abdominal operation was not advised at that time. No tumor could be felt at the time of curettage. The bleeding did not cease after the radium application, and the patient continued to flow irregularly. It was then decided that operation should be carried out in spite of her condition, so on February 17, 1935, a

supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed by one of us (L. P.). There were a few adhesions, both ovaries and the uterus being bound down into the posterior culdesac. The right ovary contained a solid tumor which was rocklike in consistency and suggested to the operator a granulosal cell tumor. The pathological report was fibroma of the ovary (fig. 12), but after

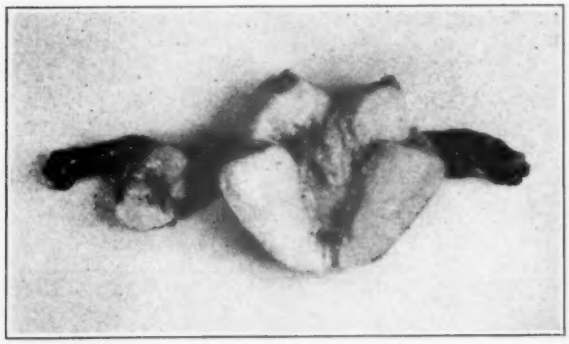

FIG. 12. *Case 3.* Photograph showing the small, firm, glistening ovarian tumor. It has been cut through the center and opened. The endometrium of the uterus is grossly thickened. This tumor is a thecoma.

reconsidering all the facts in the case and especially with the knowledge that this patient had had menorrhagia following the menopause and marked

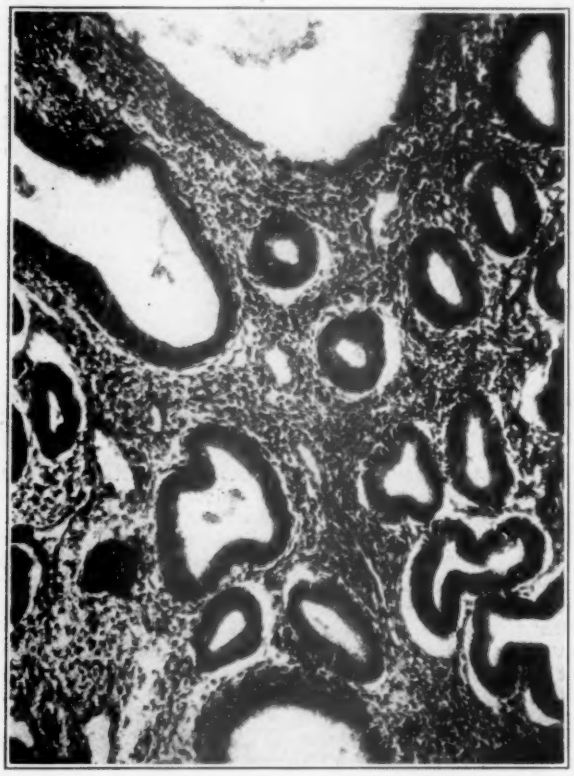

FIG. 13. *Case 3.* Photomicrograph of the endometrium showing marked estrin or proliferative effect. The glands are close together and the epithelium is full of mitotic figures. Note the areas of cystic dilatation of the glands so frequently seen in so-called Swiss-cheese hyperplasia of the endometrium.

endometrial hyperplasia, it seemed wise to assume that the tumor was one of the thecal cell types of granulosal cell tumors. The patient made an uncomplicated convalescence, and her only present complaint is obesity.

In this patient, the diagnosis of granulosal cell tumor was correctly considered. A 65 year old woman with marked hyperplasia of the endometrium (fig. 13) and menorrhagia, who was not cured by 3,500 millicurie hours of radium, should have some

FIG. 14. *Case 3.* Photomicrograph of the thecoma. Notice the firm bands of hyaline-like connective tissue. Occasionally an area of groups of cells with large nuclei that contain lipoid is seen.

sort of tumor that is capable of secreting estrin. Unfortunately complete studies were not carried out in the laboratory. Figure 12 shows the type of tumor that was removed, and the photomicrograph (fig. 14) shows the histology of the tumor. Many lipoid-containing cells that help confirm the diagnosis of thecoma are present.

## CONCLUSIONS

1. Granulosal cell tumors of the ovary are not uncommon, and surgeons, gynecologists and pathologists must be on the lookout for them.

2. There are various types of cell structures in the tumors, and three different types of granulosal cell tumors are recognized: the granulosal cell type, the luteoma and the thecoma.

3. The presence of amenorrhea, menorrhagia, high urine estrin, endometrium of the estrin phase and a tumor should give a clue to the diagnosis.

4. Precocious genital and breast development and early onset of menstruation should suggest the presence of the tumor.

5. In women past the menopause, menorrhagia or metrorrhagia, with a palpable tumor and hyperplasia of the endometrium, makes a search for such a tumor reasonable.

6. Benign tumors of the breast in youth or old age, and even in adult life, should suggest consideration of such a tumor.

7. These tumors are usually benign but may be malignant; in older women radical surgery is the treatment of choice.

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# VERMONT STATE MEDICAL SOCIETY

## THE FACTOR OF MENTAL STRESS IN ESSENTIAL HYPERTENSION*

BY ROBERT STERLING PALMER, M.D.†

KNOWLEDGE of essential hypertension has been confined almost exclusively to the unfortunate end results, the statistical chances of different eventualities after varying periods of time and the morbid anatomy and pathologic physiology of a wornout heart and badly sclerosed blood vessels. Innumerable causes have been suggested and more or less fruitlessly investigated. Many conclude that a familial tendency and an increase of years are the only known etiologic agents. That the disease results from constitutional susceptibility plus the cumulative strain of life is apparent, but I believe that the increasing knowledge of the peripheral circulation and its nervous mechanism may be leading us to a more fundamental understanding of essential hypertension.

Normal blood pressure depends not only on the head of pressure but on the peripheral resistance, blood volume and viscosity. The head of pressure may well be the least important as a first cause, since a very high blood pressure is often maintained through attacks of congestive (central) heart failure, even up to the moment of fatal termination. Most investigators agree that alterations in blood volume and viscosity are not significant in essential hypertension.

The tone of the arterioles is chiefly controlled by nervous impulses that are conveyed by the sympathetic nervous system from the vasomotor center in the medulla, which, in turn, receives a constant stream of sensory impulses from the periphery. Finally, this reflex is modified, either inhibited or excited, by influences from the higher centers. An illustration of the continuous action of this reflex in maintaining vascular tone is the marked fall in blood pressure following spinal anesthesia. Reflex inhibition may occur from a blow on the abdomen. Inhibition may arise from higher centers, as in psychogenic fainting. Finally, as will be demonstrated below, influences from the higher centers commonly cause marked elevations in blood pressure. In the minute vessels or arterioles just before the capillaries, the gradient of pressure falls sharply. These vessels evidently act as a barrier or dam, maintaining a reservoir of effective blood pressure. The capillaries, while to some extent under vasomotor control, respond by vasodilation or constriction chiefly by local reflexes according to tissue needs. The capillaries seem to constitute the mechanism for tapping the reservoir of available pressure above the arterioles. At the onset of physical activity, or with emotional stress, the reservoir of available pressure is reflexly increased by a combination of arteriolar constriction and increased cardiac output, or by maintained tone of the arterioles with an increase in the head of pressure. In the face of emergencies, the increase in blood pressure is great and is accompanied by a mobilization of the red cells and a rise in blood sugar. This emergency response is called forth by critical situations and is accompanied by manifestations of fear or rage (Cannon[1]).

If this reflex control of arteriolar tone is

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abolished by extirpation of the entire sympathetic nervous system, as was done by Cannon[1] in the cat, the blood pressure is maintained, and all ordinary bodily functions proceed, but with one important difference. There is no mechanism or only a very inferior, poorly integrated one for emergency reactions. The peripheral resistance has shifted, as it were, one step farther to the periphery and depends only on capillary resistance governed by local vascular reflexes in response to tissue needs. There is no preparedness, no fight or flight mechanism and no increase of blood pressure for emergencies. The recent work of Prinzmetal and Wilson[2] may be interpreted in this light. They showed that after novocaine nerve block, which abolishes the sympathetic outflow to the arm, the increase in blood flow was no greater in hypertensives than in normal individuals. Here again, in one limb the first barrier was abolished, and the entire resistance then depended upon the local capillary reflexes. It would not be anticipated that more blood would be forced through the part than the resting tissue actually needed.

The characteristics of the blood pressure responses at all stages of essential hypertension, which are especially well marked in the earlier cases before vascular sclerosis has occurred, are, first, marked spontaneous variability and, secondly, marked pressor response to mental stress. At first, transient rises in blood pressure occur at intervals, but they continue with ever greater facility and with more frequency, until the emergency response becomes habitual. A milder degree of the same process is seen as a normal condition in young adults of 18 to 24 years. A significant number of males at this age show systolic blood pressures over 140 mm. of mercury and are more nervous than their fellows, but they do not have a family history pointing to the presence of the constitutional factor predisposing to degenerative vascular disease.[3] The blood pressure spontaneously regresses in the majority of such patients. They have vasomotor instability, not essential hypertension. They are active, healthy, overmobilized youths, with their emergency mechanism on the stretch, as indicated by flushing, wide pupils, active sweat glands, rapid pulse and generally acti-

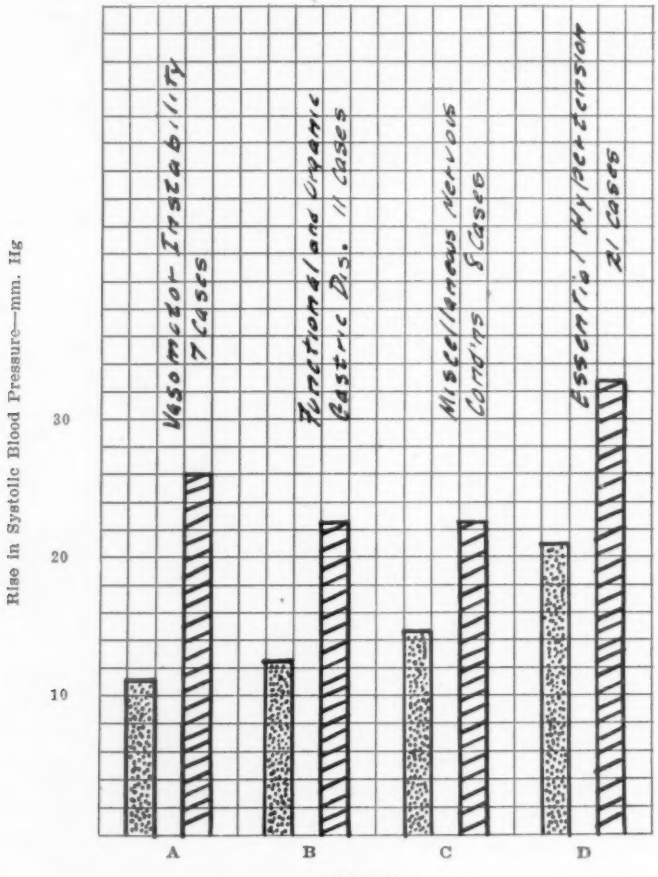


FIGURE 1.

Rise in systolic blood pressure in response to mental stress (dotted columns) and in response to immersion of the opposite hand in ice water (cross-hatched columns) shown in cases with vasomotor instability, functional and organic gastric disturbances, and miscellaneous nervous conditions (control cases) and in cases with essential hypertension.

vated expression. In response to mental stress, the blood pressure of these individuals rises an average of 11.4 mm. and, if stimulated by plunging one hand in ice water, according to the technic of Hines and Brown,[4] it rises 26.7 mm. (fig. 1 A). The results are about the same with any normal control except that at a corresponding age the less activated individual responds less violently. If we use as controls patients with gastric disorders, both functional and organic, or a miscellaneous group made up of patients with nervous fatigue, effort syndrome, thyrotoxicosis, and the like, we find that the average response to mental stress is 12.5 and 14.5 mm., while the response to cold is 22.7 and 22.6 mm., respectively (fig. 1 B and C). In essential hypertension, on the other hand, the average response to mental stress is a rise in systolic blood pressure of 21 mm., while the average response to cold is 32.5 mm. (fig. 1 D). It is apparent that the response to both mental stress and to cold is greater in hypertensive individuals than in the controls or in those with vasomotor instability. Those with vasomotor instability, however, do show a greater response to cold than the control groups.

It is, of course, highly desirable to make an early diagnosis of essential hypertension, even in the so-called prehypertensive state, and it was thought by Hines and Brown[4] that the cold test might do this. However, I have found pathologically exaggerated responses to cold in patients with gastric disorders and low blood pressures, in psychoneurotics and in others (fig. 2 C). Nevertheless, in certain young patients with marked vasomotor instability and with a normal or only slightly elevated blood pressure, response to cold is greater than in controls (fig. 2 B). The response of a normal person to mental stress and to cold is shown in figure 2 A, the typical response in a hypertensive patient in figure 2 D. That the level of the systolic blood pressure alone is not responsible is shown in figure 2 E, which demonstrates the response to mental stress and to cold of a patient with coarctation of the aorta, who suffered from a nervous fatigue syndrome.

From fairly close and continued clinical follow-ups and from approximately 100 blood pressure observations of this sort on 21 hypertensive patients, 7 patients with vasomotor instability and 18 control patients with normal blood

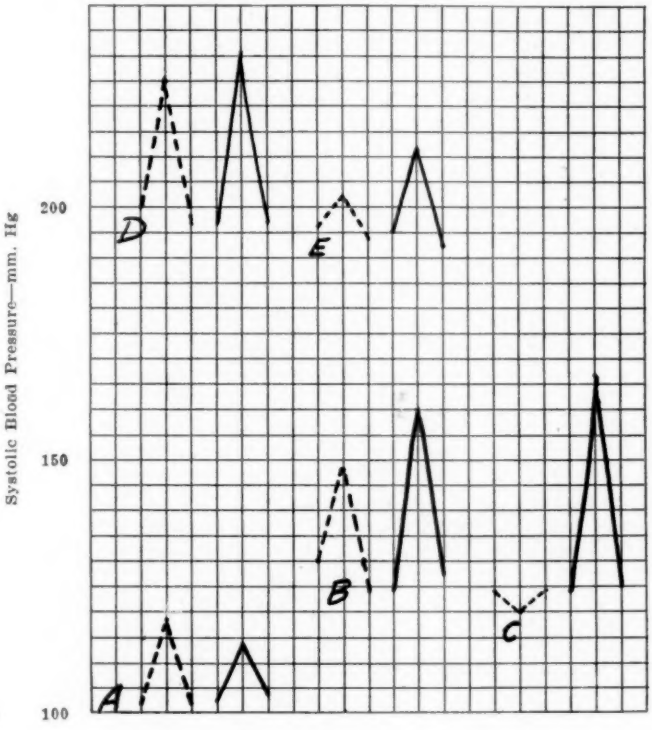


FIGURE 2.

The reaction of systolic level of blood pressure to mental stress (broken line) and to immersion of the opposite hand in ice water (solid line) in:

A. Normal control.
B. Young woman with vasomotor instability.
C. Patient with duodenal ulcer with recent exacerbation of symptoms.
D. Female patient, aged 48, with essential hypertension.
E. A patient with coarctation of the aorta.

pressures, but with functional or organic disease (peptic ulcer) in which mental stress was a prime factor, the evidence is suggestive that essential hypertension depends upon constitutional susceptibility, possibly an unduly sensitive sympathetic nervous system, and nervous strain. In my experience, most of these young adult patients with vasomotor instability do not develop essential hypertension in the course of 10 years.[3] The patients in this group that do develop essential hypertension may have a strong family history of degenerative vascular disease. In addition to the constitutional tendency, the precipitating factor of mental stress cannot be overemphasized. Those who have definite essential hypertension usually have experienced severe and prolonged mental or nervous strain and often have suffered from insomnia, functional gastric disorders, marked exhaustion and, occasionally, more or less severe nervous breakdowns. The younger patients are often very highly sexed, sometimes with unsatisfactory outlets. Others have been unduly active sexually.

It may be significant that a rise in blood pressure normally occurs at puberty,[5] and that essential hypertension is so commonly associated with the menopause in women and with the time of life when vigor is waning in men. These epochs are not only physiologic but they involve important changes and stresses for the whole personality. A boy while in college and at graduate school had a systolic pressure of 160 and was conscious of inner nervous tension and anxiety, not only about his blood pressure, but about other things. In the 3 years since leaving school he has spontaneously developed increased stability accompanied by self-confidence, and his blood pressure is at present 130. Another man of 38, while overworking and overplaying a year ago, experienced throbbing, palpitation, headache, insomnia and anxiety states; his blood pressure was 190. With rest and good hygiene, his blood pressure now is 135. Will such patients in middle life or later, with the

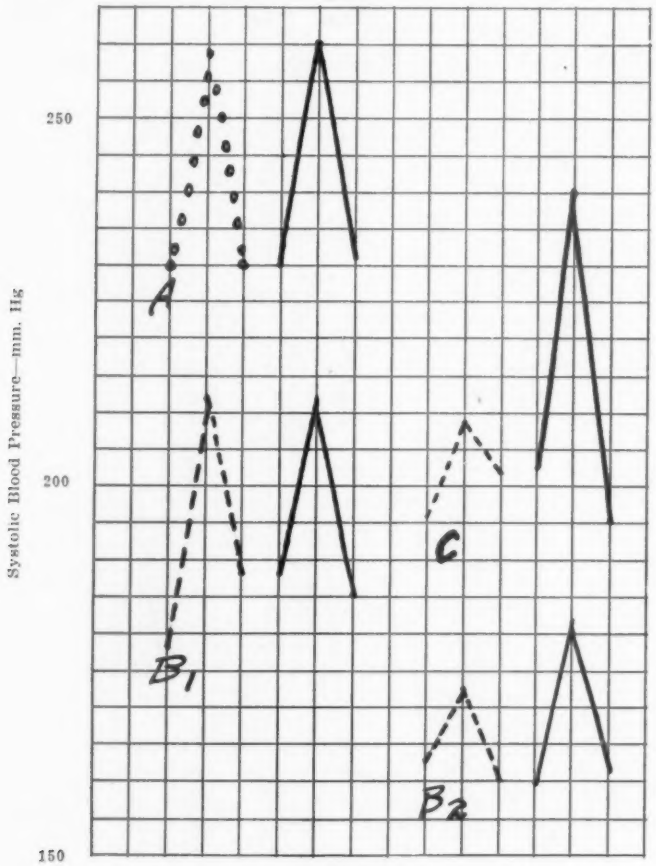


FIGURE 3.

A. Rise in systolic blood pressure in response to spontaneous memory of a painful event (circles) and in response to cold (solid line) in a case of essential hypertension.

B. 1. Response to mental stress (broken line) and to cold (solid line) in a case of essential hypertension.

2. Same after sedation, psychotherapy and voluntary relaxation.

C. Response to mental stress (broken line) and to cold (solid line) after a cerebral accident causing hemiplegia in a male, aged 56, with essential hypertension.

strains and adjustments of that period, develop essential hypertension? May it be prevented now? These are questions that cannot be answered at this time. One can at least avoid fixing anxiety on the blood pressure. These patients may be relieved of special sources of anxiety with favorable results. Apparently analytic psychotherapy, especially in certain young adults, may be very effective.[6, 7]

In the fully developed case of essential hypertension, nervous factors are prominent, and the pressor effect on the level of the blood pressure is marked. Figure 3 A shows the blood pressure response to spontaneous mental stress and to cold in a typical case of essential hypertension. While a series of blood pressures were being taken, the patient spontaneously recalled an automobile accident in which a child was severely injured and which he had witnessed a few days before. Figure 3 B 1 shows the response to mental stress applied by questioning in regard to a painful personal experience and the response to cold in a typical case of essential hypertension. It is possible that the patient with essential hypertension, being especially susceptible, may acquire a conditioned reflex—the emergency response of the blood pressure, which habitually becomes induced by less intense stimuli. This response may be modified by a regimen including rest, sedatives, psychotherapy and training in voluntary relaxation, as shown by the responses of the same hypertensive patient to mental stress and to cold before (fig. 3 B 1) and after (fig. 3 B 2) treatment. One or two observations show a diminished response to mental stress after a cerebral accident (fig. 3 C). The unaccustomed calm and mental quietness of the patient after such an attack is sometimes quite noticeable.

If a vasomotor reflex of the sort described is the basis of essential hypertension, how may it be modified? Cutting down peripheral impulses and increasing inhibition from the higher centers by rest, conscious relaxation, psychotherapy and sedatives are quite effective in many cases.[8] These measures bring symptomatic relief in 90 per cent of mild cases, 75 per cent of moderate cases and 46 per cent of late cases, while a substantial fall in the blood pressure is obtained in 50 per cent of the mild and moderate cases and in 33 per cent of the severe cases. We have learned to look for certain cases with a tendency to advance rapidly and which occur in patients under 50 years of age, particularly in women. In these patients and in those where a medical regimen is ineffective or cannot be followed, surgery of the sympathetic nerves, which interrupts the reflex on the efferent side, while still in the experimental stage, appears to offer some possibilities. In our hands, within the limits of 1½ years' observation of 25 cases, splanchnic resection has been very successful in young adults, returning the blood pressure to normal in early cases, lowering and stabilizing the blood pressure in moderate cases, but having no effect on the blood pressure in late and malignant cases. As long as the case is still in the vasomotor stage, the operation appears to be successful, but it is only partially so or a failure in others. In those cases in which a cure has not been obtained two possible explanations present themselves. Arteriolar sclerosis may be sufficiently advanced to prevent relaxation or, in moderate and advanced cases, habitual local precapillary resistance, mainly under local nervous reflexes, may have developed and is not altered by diminishing the sympathetic outflow.

## CONCLUSION

Essential hypertension is considered as a "chronic emergency" response of the organism. It depends upon nervous strain in an individual with a constitutionally susceptible sympathetic nervous system.

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# HUMAN AUTONOMIC PHARMACOLOGY. IV. THE EFFECT OF BENZEDRINE SULFATE ON THE GALLBLADDER*

BY PURCELL G. SCHUBE, M.D.,† MAX RITVO, M.D.,† ABRAHAM MYERSON, M.D.,† AND RUTH LAMBERT, A.B.†

BENZEDRINE sulfate (phenylisopropylamine sulfate) is a synthetic preparation belonging to the ephedrine-epinephrine group of drugs. According to Tainter[1] its primary action is to stimulate the sympathetic division of the autonomic nervous system. Physiologically, it raises the blood pressure for prolonged periods,[1, 2, 3, 4, 5] the rise in systolic pressure being greater than that of the diastolic;[5] it decreases the pulse rate, except in some instances where it may have the opposite effect;[5] it produces a constriction of the blood vessels of the upper respiratory tract[6, 7, 8, 9] and of the organs acting as reservoirs for red blood cells;[4] it increases the intracranial pressure;[4] it stimulates the central nervous system;[4, 10, 11, 12, 14] it increases the acidity and the pepsinogen content of the gastric juices;[13] and it relaxes the tonus of the gastrointestinal tract.[15]

Our plan is to extend the investigations on the effect of benzedrine sulfate on the gastrointestinal tract and to study its action on structures intimately allied to it. It is the purpose of this paper to evaluate the effects of the drug on one of these structures, the gallbladder.

## METHOD

The individuals used in this study were all mentally ill but free of any clinically demonstrable organic pathology. All were males and ranged in age from 18 to 45 years. Each patient was used as a control on himself and on the entire group.

*Control Study.* Before the benzedrine study was started, each patient received a gallbladder dye test to determine the size and rate of emptying of this viscus. The night before the test the patient received a light meal, which consisted of dry toast, tea and sugar. One hour later he was given the gallbladder dye, tetra-iodo-phenolphthalein sodium, orally. The following morning, after a fast of at least 15 hours, x-ray films were taken of the gallbladder region. He was then given a meal rich in fat, which consisted of two slices of white bread thickly spread with butter, and two glasses of a milk and cream mixture into which had been beaten four raw eggs. After a lapse of 1 to 2 hours, x-ray films were again taken. Only those individuals were used in whom there was either a marked diminution or complete absence of the gallbladder shadow on the x-ray films that had been taken after the fatty meal. This method of dye administration and type of meal were used throughout the work.

*Benzedrine Sulfate Study.*

Group 1. In this series of 6 cases, the patient was given 30 mg. of benzedrine sulfate subcutaneously after the initial x-ray films of the dye-filled gallbladder had been taken. One-half hour after the administration of the drug films were again taken, and the patient was immediately given the fatty meal. The films were then repeated at 30 and 60 minute intervals.

Group 2. In this series of 2 cases, after initial x-ray films had been taken, the patient was given 30 mg. of benzedrine sulfate subcutaneously, and subsequent x-ray studies were made 15 and 30 minutes and 1 and 2 hours after the drug had been administered. Each patient was then given the fatty meal and the films repeated in 2 hours.

Group 3. In this series of 7 cases, after the control films had been taken, the patient was given 30 mg. of benzedrine sulfate subcutaneously. Subsequent x-ray studies were done at 1 and 2 hour intervals after the injection of the drug. Each patient was then given a fatty meal, and the films were repeated within 2 hours.

## RESULTS

Charts 1, 2 and 3 represent tracings of the gallbladder shadows as visualized on the x-ray films of the patients in groups 1, 2 and 3, respectively.

Group 1. The effect of benzedrine sulfate on the dye-filled gallbladder was studied in these patients before the administration of the fatty meal. The x-ray films that were taken 30 minutes after the drug had been given showed little, if any, change in the size of the gallbladder shadow. In 3 of the patients, there appeared to be a slight increase in the size of the gallbladder shadow, but this was not marked. The fatty meal was given to the patients 30 minutes after the drug had been administered, and subsequent films showed a gallbladder shadow in only 1 patient.

Group 2. In this series of cases, the effect of benzedrine sulfate on the dye-filled gallbladder was studied at frequent intervals over a 2 hour period before the administration of the fatty meal. Films taken 15 and 30 minutes and 1 and 2 hours after the drug had been given

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showed no important changes in the size of the gallbladder shadows. The fatty meal was given to each patient 2 hours after the drug had been administered, and subsequent films showed a gallbladder shadow that was somewhat decreased in size but very definitely present in each case.

Group 3. In these patients, the effect of the benzedrine sulfate on the dye-filled gallbladder was studied at 1 and 2 hour periods after the drug had been administered. The x-ray films taken at these periods showed the size of the gallbladder shadow to be unchanged in 3 cases, slightly smaller in 2, and slightly larger in 2. The fatty meal was given to each patient 2 hours after the drug had been administered, and subsequent films showed the gallbladder shadow to be absent in only 1 patient. Of the 6 patients in whom the shadow was present, the size remained unchanged in 3; it became slightly smaller in 1 and slightly larger in 2.

CHART 1. Tracings of the gallbladder shadows of group 1.

## DISCUSSION

In this study, several facts have been established that are relative to the effect of benzedrine sulfate on the gallbladder. This drug does not of itself cause the gallbladder to empty. In no patient was the gallbladder found to decrease materially in size after the administration of the drug. The drug did not inhibit or prevent the emptying of the gallbladder after a fatty meal, when the meal was given at the height of the drug action, that is, 30 minutes

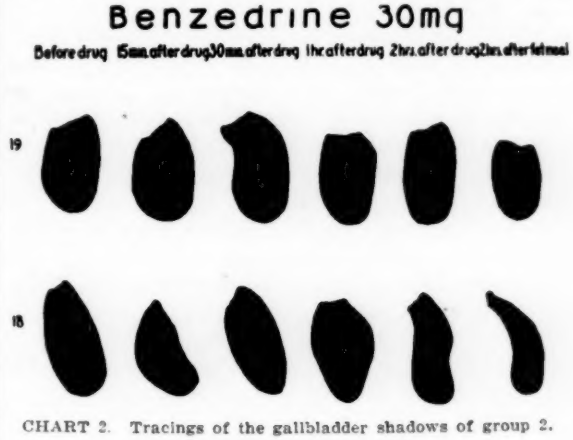


CHART 2. Tracings of the gallbladder shadows of group 2.

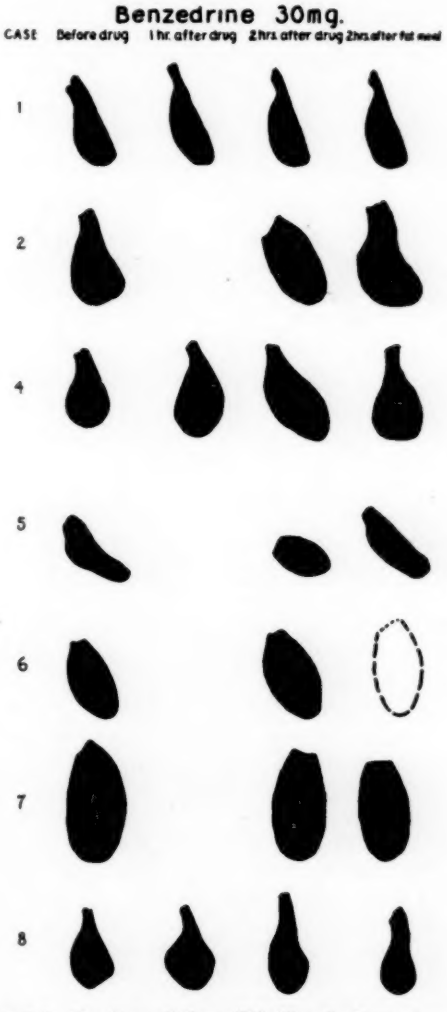


CHART 3. Tracings of the gallbladder shadows of group 3.

after its administration. In 1 patient, the gallbladder did not empty, but, when this result is considered in conjunction with the other material, it can only be felt that this inhibition was an exception to the general findings and an expected individual variation in experimental work. When benzedrine sulfate was given to an individual, and a fatty meal was consumed by him 2 hours later, there was a very definite delay in the emptying of the gallbladder. This was true in all but 1 case and it must again be assumed that this case was an individual variation.

The influence that benzedrine sulfate exerts on the gallbladder is, therefore, a definitely delayed one. That this is true is established by the fact that most of the other physiologic effects of this drug usually become evident a short time after it is administered and reach a peak of effect in 30 to 60 minutes, after which the effect rapidly wears off. The outstanding exception to this is the effect of central stimulation, which may last many hours. It is hardly possible that there is a direct connection between this stimulation and the inhibition of the emptying of the gallbladder as has been described, so it will be necessary to seek elsewhere for an explanation of the results on the gallbladder.

At the present time this is rather difficult inasmuch as the physiologic mechanisms that produce emptying of the gallbladder are imperfectly understood and not unquestionably established upon a sound scientific basis.

The existing literature relative to the problematical mechanisms that cause emptying of the gallbladder indicates that (a) there is a reciprocal innervation of the gallbladder musculature and the sphincter of Oddi and, when the gallbladder contracts, this sphincter relaxes; (b) the gallbladder has a musculature sufficiently powerful to be capable of producing the amount of contraction necessary to empty it, and it does so periodically; (c) the innervation of the gallbladder is autonomic, as parasympathetic stimulation will induce contractions of the gallbladder wall; (d) there is possibly a hormone, cholecystokinin, which is liberated from the duodenal mucosa upon the contact of this mucosa with stomach contents, and which induces the emptying of the gallbladder; (e) there is a direct chemical stimulation by substances such as egg yolk and fats, which causes the emptying of the gallbladder. In addition, there is an extensive literature pointing to the existence of an intimate relation between the stomach, the pancreas and the liver in the emptying of the gallbladder.

Just where benzedrine acts upon the digestive apparatus to establish its effect is, at this stage of our work, unknown. We do know, however, that it relaxes the gastrointestinal tract[5] and that it increases the free hydrochloric acid in the stomach,[13] by sympathetic stimulation. Whatever effect is obtained upon the gallbladder, one would expect it to be the result of sympathetic stimulation. Yet, when the action of the drug was at its height, 30 minutes after its injection, the gallbladder in most of the cases emptied normally after a fat meal, and it was only after the drug had been permitted to act for at least 2 hours that the administration of the fat meal did not empty the gallbladder. It can only be postulated, therefore, that the effect of the benzedrine on the gallbladder is a delayed one. When benzedrine is administered, its action on the gallbladder is not immediate (within 30 minutes), but it acts after many of the other benzedrine effects have disappeared. It is very probable that the failure of the gallbladder to empty after benzedrine has acted for some time may be due to (a) the failure of the stomach to empty normally because of atonicity or of failure of some essential chemical substance to be elaborated in the stomach, which, when in the duodenum, stimulates the chemical or hormone action necessary to empty the gallbladder or because of both or (b) the relaxation of the walls of the gallbladder due to drug sympathetic stimulation or to direct contact of the walls with the drug. It is not felt that the failure of the gallbladder to empty after the drug had acted for some time was due to an interruption of the reciprocal innervation of the gallbladder and the sphincter of Oddi, because at no time did we observe any gallbladder to be actively contracting.

Clinically, this work would seem to indicate that (a) there is no contraindication to the use of benzedrine sulfate in spastic gallbladder disease or in cholelithiasis; (b) benzedrine can be given to individuals who are having gallbladder studies done, provided the drug is given about one-half hour before the fat meal; (c) emptying of the gallbladder by a fat meal can be prevented, provided that benzedrine is given 2 hours before the meal.

## SUMMARY

A study of the effect of benzedrine sulfate on the gallbladder is presented.

It has been shown that when a fatty meal has been administered within 30 minutes after the drug, the gallbladder empties normally, but that when a fatty meal is given at least 2 hours after the drug, the gallbladder fails to empty.

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# TREATMENT OF CONSTIPATION

BY ALLEN G. BRAILEY, M.D.*

IN an earlier paper,[1] I described a method of treating constipation, which was based on the assumption that the normal, regularly recurring call to stool is a habit which can be acquired by almost everyone at the price of faithful adherence to a definite training schedule. The present paper is a report of the results of this method of treatment in a series of 100 consecutive private patients who gave constipation as a major complaint.

Most of these patients also complained of belching, heart burn, coated tongue, headache after meals and a sense of lassitude, often referred to as "indigestion".[2, 3] Such symptoms are probably due to mild degrees of reverse peristalsis,[4, 5] the result of chemical or mechanical irritation of the intestinal mucosa, or to abnormal nervous stimuli, such as may occur with emotional stress. If this explanation is correct, it is easy to understand why permanent benefit is not obtained by the use of additional irritants, of which purgatives and high roughage diets are probable examples. The body shows a strong tendency to return to a normal state of tone and function and the best care often consists in removing the hindrances to this normal restorative process. This principle has been kept in mind in dealing with patients with these functional intestinal troubles.

## PLAN OF TREATMENT

In starting treatment, the following instructions were carefully explained and were also written out for each patient:

Have strictly regular habits for:

1. Sleep—a regular time for rising and, insofar as is practicable, for going to bed.
2. Meals—no eating between meals (no unusual amount of roughage).
3. Fluids—at least 8 full table glasses daily (milk, fruit juice, water, and so forth).
4. Exercise — at least 30 minutes daily (strenuous enough for some breathlessness and palpable perspiration).
5. Toilet visit—stay 15 minutes, if necessary, without straining; if possible, ignore calls to stool at any other time; no laxative or oil is allowed, but, if 3 days elapse without any sort of stool, take a small, warm water enema at the end of the usual toilet visit on the third day.

This concession concerning the enema was made for two reasons. First, in spite of assurances and explanations, an occasional patient faces a future without cathartics with the feeling that he has had his last stool, and it reassures him to think that he may have an enema if his fears seem likely to be realized; *but it is allowed only after 3 days of failure.* Secondly, there is an occasional patient with whom several days may pass before the bowel will empty itself spontaneously and, if allowed to wait too long, his first stool may be so firm as to cause harmful stretching of the anal mucosa. Actually, an interval of 3 days without a stool has seldom occurred, and more than one enema has been very rarely required.

## RESULTS

Of the series of 100 patients treated, 1 was not helped and another is only partly relieved. The rest are all cured in the sense that each has reported passing normal stools of normal consistency at a regular time daily, without effort and without laxatives or lubricants. At the same time their "indigestion" has been greatly improved and usually has disappeared altogether. The time required to establish this regular stool habit has been from a few days to a few weeks—usually about 2 weeks. I have found no clinical evidence that the prolonged use of cathartics

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produces any permanent irritative, atonic or other changes in the intestinal mucosa or musculature. The cathartic habitué was relieved as readily as was the novice.

I do not wish to appear to oversimplify this problem. Even when organic disease has been ruled out, many factors of the environment, personality and emotional make-up must be considered, and each patient requires sympathetic and individual thought. To toss the patient hurriedly a sheet of instructions instead of a laxative will not prove a very superior substitute for the latter. I wish to emphasize strongly, however, that lack of satisfactory habits is the chief source of trouble, and that laxatives, oils and enemas are almost never required and are apt to cause more symptoms than they relieve.

## CASE REPORTS

*Case 1.* A housewife, 63 years of age, had been constipated since youth and stated that she had not defecated more often than twice each month for 25 years, in spite of taking from one to three laxatives in therapeutic doses practically every night. She was remarkable in that she seemed very insusceptible to intestinal irritation; physics gave her no stools and no indigestion. She wanted treatment because she did not want to be abnormal and because she was afraid of auto-intoxication. She was very incredulous of the value of the treatment outlined but was willing to try it. She had three stools the first week and 3 weeks later she had established a normal, regular, daily stool. She reported 6 months later that she continued to be perfectly normal, regular and well, with respect to her intestinal tract.

*Case 2.* A housewife, 30 years of age, was well until the birth of the second of her two children, 7 years ago. Ever since leaving the lying-in hospital she had taken daily cathartics. Her physical examination showed no organic disease. The instructions outlined above were given, and she was asked to report results in 2 weeks. After 10 days she telephoned that her stools were already entirely normal, and she was excused from making a second visit. The physician who referred her told me 6 months later that she had had no recurrence of difficult stools and was very happy over the result.

It seems certain that this person had nothing but a bad laxative habit, which was undoubtedly started by the use of enemas or laxatives while in the hospital. Her history illustrates the remarkable persistence of habits once formed, whether they be bad or good.

*Case 3.* A public accountant, 40 years of age, complained of constipation, indigestion, and frequent and severe headaches since childhood. A complete physical examination was negative except for myopia, which was properly corrected by glasses. His treatment in the past had included special diets, a modified Sippy regime and a wide variety of laxatives and oils. He had had his tonsils removed and his teeth x-rayed for possible foci of infection. A gastrointestinal series, Graham test and barium enema showed no organic disease.

Two weeks after starting treatment, he reported regular, daily stools, very much less heart burn and distress from gas and fewer headaches. One year later his bowel habits were still normal, and he had had headache or abdominal distress on only one or two occasions.

*Case 4.* An unmarried schoolteacher, 56 years of age, complained chiefly of classical attacks of migraine for 40 years. She had considered herself constipated since childhood and had taken physics of some sort almost daily. Twenty years ago a surgeon had performed a laparotomy for the removal of a Lane's kink. A complete physical examination showed only undernourishment and moderate hypertrophic arthritis.

She was started on the program of good hygiene given above and was told to stop all laxatives. Two months later her stools were normal; she had had only one mild and abortive headache and had gained 6 pounds in weight. For 3 years she has reported continued good health and freedom from headaches. No claim is made that this treatment cured her migraine. Her migraine might well have subsided spontaneously before reaching the age of 56. She was very obviously benefited by better living habits, however, and her lifelong habit of constipation was easily and quickly broken.

*Case 5.* A housewife, 54 years of age, had had constipation for years and almost daily abdominal distress, distention and pyrosis. She stated that her bowels had "never moved without a physic." She had had attacks of suprapubic pain after urination for many years, and treatment for this condition had not been helpful. She was very unstable emotionally, nervous and tense. She had had a stormy experience with the menopause, the vasomotor disturbances of which still annoyed her at times. A careful physical examination showed no organic defect.

She adopted the treatment advised and stopped all cathartics. One week later she reported that her bowels had not moved, but, to her great astonishment, her indigestion had disappeared, and her bladder symptoms were very much better. She continued to improve, and her stools became essentially normal, but occasionally she still takes one teaspoonful of plain mineral oil.

This is the person referred to above as only partly relieved. She considers herself much better than before she started treatment, but her emotions continue to be easily upset by circumstances that neither she nor I can control, and each such upset brings some slight recurrence of her old symptoms.

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# CASE RECORDS
## *of the*
# MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

## CASE 23161

### PRESENTATION OF CASE

A 67 year old American college instructor was admitted complaining of attacks of substernal discomfort.

About 2½ years before entry the patient began to have occasional attacks of what he termed indigestion. These attacks consisted of a constricting sensation beneath the upper portion of the sternum and were occasionally associated with a similar sensation in the posterior portion of the chest. The attacks were precipitated by moderate exertion, such as climbing a hill, and were usually relieved by a brief rest. During the year preceding admission he noted gradually increasing dyspnea, which was evident while talking and which, on occasions, awakened him from sleep. He had always had a slight, dry cough, which did not increase in severity. There was no edema. During his illness he lost weight, but the exact amount was not recorded. A week before coming to this hospital he was awakened shortly after going to bed by a severe paroxysm of coughing, which continued for about an hour and was productive of moderate amounts of phlegm flecked with blood. He developed a sensation of pressure in his chest, which radiated to the left shoulder. Pertinent details were not recorded, but the discomfort continued and prevented him from sleeping. There was no further discomfort the following day, but that night he was again unable to sleep because of nausea and the repeated raising of blood-tinged phlegm. There was no cough at that time, but he was markedly dyspneic and apprehensive. He entered a hospital where his breathlessness was controlled by morphine and digitalis. While in the hospital his temperature was 100°F., and his pulse was irregular, with a rate of about 115. The fever continued until shortly before entry to this hospital. There was profuse perspiration during this period.

Five months before admission a scrotal operation had been performed and one testis removed. The reason for this operation was not known.

Physical examination showed a perspiring, orthopneic, elderly man with ashen cyanosis. His respirations were Cheyne-Stokes in character, and his skin was cold and clammy. There was moderate sclerosis of the retinal arterioles. The cardiac impulse was diffuse and wavy in character and extended over an area about 7 centimeters in diameter. The left border of cardiac dulness extended 12 centimeters to the left of the midsternal line. There was gallop rhythm. The sounds were of poor quality. A blowing, systolic murmur was audible in the apical region and was transmitted into the axilla. The blood pressure was 150/110. Chest resonance was unimpaired, but many fine, moist rales were audible at both bases. There was moderate sclerosis of the peripheral vessels, but no edema.

The temperature was 100°F., the pulse 100. The respirations were 25.

Examination of the urine showed a specific gravity of 1.024. There was a trace of albumin. The sediment contained rare red and white blood cells. The blood showed a red cell count of 4,200,000, 85 per cent hemoglobin. The white cell count was 11,000, 76 per cent polymorphonuclears. The sputum was mucopurulent in character and contained no tubercle bacilli. The nonprotein nitrogen of the blood was 38 milligrams per cent. A blood Hinton test was negative. An electrocardiogram showed left axis deviation, diphasic $T_1$ and $T_2$ and high origin of $T_4$.

A portable x-ray film of the chest showed mottled dulness involving almost the entire area of both lung fields. Mottling was confluent along the right border of the heart, where there was a triangular area of density. The right upper lobe appeared to be reduced in size. There was a small amount of fluid at both bases. The heart was grossly enlarged in all diameters. The predominating enlargement was in the region of the left ventricle. The aorta was obscured by dulness in the lung, but there was dilatation of the vena cava and pulmonary vessels.

The patient's temperature varied between 98.6 and 100°F. during the first 2 weeks in the hospital, and his white count on one occasion rose to 17,000. Notes by several observers stated that rales were more evident in the upper anterior portion of the right chest. No definite dulness was elicited. The blood pressure rose to 180/110 but later went down to 140/110. The gallop rhythm persisted, and there was pulsus alternans. After the end of the second hospital week the temperature remained elevated between 100 and 102.5°F. The patient, who had remained in a precarious condition despite the administration of oxygen, digitalis and sedatives, became progressively weaker and died on

the twenty-fourth hospital day. There was no note of pain or cough during the period of hospitalization.

### X-ray Interpretation

Dr. Aubrey O. Hampton: These are portable films taken with the patient lying on his back. The supracardiac shadow and the aortic arch are magnified. This is the triangular area of density that is mentioned. There is mottling all over the midareas of both lungs and in the upper lobe on the right. The right upper lobe is reduced in size, and a few lesions have the appearance of old scars. I do not know how we can be certain that the right upper lobe is not reduced in size from bronchial occlusion. It would be very unusual to see it at this stage. The scarring in the right upper lobe could be due to old tuberculosis.

Dr. Alfred O. Ludwig: Are there any adhesions there?

Dr. Hampton: Yes, pleural adhesions.

Dr. Ludwig: What about the mottling? Do you think it is due to passive congestion of the lung?

Dr. Hampton: I think that it suggests an infarct, and perhaps some of the other areas of dulness are from infarcts also.

Dr. Ludwig: Would you think of malignancy at all?

Dr. Hampton: The lung roots do look large. We thought that these shadows at the lung roots were blood vessels. The picture could be produced by passive congestion.

Dr. Ludwig: Is there any evidence of right auricular enlargement?

Dr. Hampton: There is diffuse enlargement of the heart; the greatest change is in the region of the left ventricle. That observation about the dilated vena cava might be a little inaccurate.

### Differential Diagnosis

Dr. Ludwig: This history starts off innocently enough, and there seems to be little doubt that this 67 year old man had very definite angina pectoris. His attacks as described are perfectly typical, with constriction beneath the upper portion of the sternum, which is brought on by exertion; and, from what we find about the blood pressure later on, there can be little doubt that he had hypertension and probably hypertensive heart disease, as well as definite involvement of the coronary system, which would be enough cause to give him angina pectoris. Preceding admission he began to have gradually increasing signs of a failing heart, evidenced by dyspnea and perhaps by the slight, dry cough. There is additional evidence of beginning cardiac failure, more left-sided than right-sided, of course.

The first thing that we come to of any great importance is the severe paroxysm of pain and coughing that this man had 1 week before coming to the hospital. It is interesting and important to speculate about the character of that attack. Offhand, I think one would say that it was an attack of cardiac asthma or a paroxysm of nocturnal dyspnea, coming on quite suddenly as a result of left ventricular failure. The attack does not seem typical of pulmonary edema, although it may perfectly well have been, since he raised moderate amounts of phlegm flecked with blood. This phlegm is not described as large amounts of foam flecked with blood, which one ordinarily associates with pulmonary edema. The pain radiated to the left shoulder. That could have occurred, I think, from the considerable degree of cardiac failure per se, but one wonders if something else did not happen—whether he had a coronary infarction, let us say. If he had a coronary infarction, it must have been very severe because of the degree of failure and disturbance; but then, we find he got up the next day, which does not sound compatible with a severe degree of coronary thrombosis. If it had been a relatively small infarction, he might have been able to get up the next day.

What else might this be? It occurred to me that the extreme amount of coughing was unusual for the conditions I have mentioned thus far, that is, for cardiac asthma, pulmonary edema or coronary thrombosis. It makes me think of the picture one sees in pulmonary embolism, for instance. Very often the appearance of emboli in the lungs gives just this sort of picture and may be associated with a good deal of cough, distress, dyspnea and blood-tinged phlegm.

He had another attack of the same sort on the following night. He obviously did not have another coronary infarct—I should not say "obviously"; he might well have had it, but it does not seem likely to me. He ran a slight fever, which does not help very much. He might have had a temperature with either coronary thrombosis or pulmonary infarct. The irregular pulse fits in somewhat better with coronary thrombosis, but there again we would like to know the nature of the irregularity. Was he fibrillating; did he have frequent extrasystoles; or was the irregularity due to pulsus alternans? It may have been any of these things. If he was fibrillating, I should lean more toward coronary infarction than toward pulmonary embolus. Whereas, if it were due to the other irregularities, pulmonary embolus is more likely.

Then, we have the note about the scrotal operation, which I, perhaps foolishly, am inclined to discount. I cannot see how it fits into the

rest of the story. Possibly he had a tumor of the testicle.

His physical examination is primarily what we would expect in a man of his age with hypertension and coronary heart disease with failure and, perhaps, with a recent, severe episode of, let us say, coronary thrombosis. The ashen cyanosis that one sees so often following such an episode is described, but, there again, it may have been the result of pulmonary embolism. The Cheyne-Stokes respirations are again merely secondary to whatever caused the pain and discomfort that he had the week before he came in. It is obvious from the description, or at least it seems obvious to me, that this man had a considerably enlarged heart. The cardiac dulness extended 12 centimeters to the left of the midsternal line. We do not know how large a man he was but, assuming that he was of average size, probably the heart was considerably enlarged to the left. It might be due to acute dilatation or, more likely, to left ventricular hypertrophy from long-standing hypertension. The gallop rhythm and the nature of the sounds again make us think of an acute coronary episode, failing heart from old coronary disease or hypertensive heart disease. The blowing, systolic murmur is probably explained by dilatation. It is quite surprising that, with all this disturbance coming on, he had so few physical signs in the chest. Also, it is interesting to note the complete absence of signs in the periphery; nothing is said of a large, tender liver or whether the neck veins were dilated and pulsating. There apparently was no edema. The temperature, pulse and respirations are perfectly consistent with ordinary cardiac failure, coronary thrombosis or pulmonary embolus.

The urine shows a high specific gravity, a trace of albumin and a few red and white blood cells. The nonprotein nitrogen was 38 milligrams per cent. I should interpret that as perfectly consistent with the urine one expects with cardiac failure and should say that he does not have any degree of parenchymatous nephritis. He has the high specific gravity and the slight retention of nonprotein nitrogen that we so frequently see in moderate or severe degrees of cardiac failure. As far as the electrocardiogram is concerned, my impression is that it is not of much help in making a diagnosis of past coronary disease or in deciding whether the patient had an acute coronary episode. I think that all these changes could be produced by digitalis alone. I would like to ask Dr. Sprague's opinion on that.

DR. HOWARD B. SPRAGUE: I think that the statement is perfectly true. The electrocardiographic changes do not help you in this case, and they could be produced by digitalis.

DR. LUDWIG: The other point that interested me somewhat was the number of cases of acute coronary thrombosis that did not show electrocardiographic changes before we had chest leads. I think such cases are few.

DR. SPRAGUE: The number is said to be 2 per cent, but that is based on individual tracings, not serial ones.

DR. LUDWIG: My impression is that, if there are signs of coronary thrombosis without electrocardiographic findings, one had better look for something else.

DR. SPRAGUE: I think that is true, particularly since we now have chest leads.

DR. LUDWIG: There are a few things in the x-ray films that interest me. One is the curious mottling, which may be due to chronic passive congestion of the lungs alone; however, we wonder if it may be due to anything else. Then, there is this curious area of density, and, thirdly, the cryptic note about the vena cava and the pulmonary vessels. All these may be simply misleading, but, on the other hand, they may be important. It occurs to me that mottling may be due to other causes. What are these other causes? I have already mentioned pulmonary embolism. It is conceivable that this man may have had multiple, small, pulmonary emboli, and that this area may be an infarction resulting from a large pulmonary embolus. You may say that he does not have any focus to produce emboli. That does not rule out a focus by any means. Phlebitis, without signs, may be a source. Furthermore, an irregularity of his heart at some previous admission is described. It may have been previously fibrillating and could have produced pulmonary emboli; but, if he had pulmonary emboli, they would more likely have been produced from pelvic phlebitis than from the heart.

One other thing occurred to me. It may be somewhat of a flight of fancy, but this may be some sort of metastatic carcinoma. I was quite interested to run across an article that described a picture similar to this man's. In the 4 cases described, 3 patients had carcinoma of the stomach, and 1 had carcinoma of the sigmoid. They presented a diffuse lymphatic metastasis in the lung, and it was postulated that the tumor got into the lung either through the hepatic veins into the vena cava or through the thoracic duct into the vena cava and spread out to the lymphatics and periarterial lymphatic channels, causing a tremendous amount of increased resistance in the lesser circulation. Apparently the radiologists were able to make this diagnosis by x-ray alone. I have never seen such a case, but it is possible that this man represents one. Certainly we have no right to say that this man had a carcinoma, because he has no symptoms or signs. On the other hand, one sees cases of carcinoma of the stomach without symptoms or signs. Then, the dilated vena cava and pulmonary vessels, if

my theory is correct about something obstructing the lesser circulation, are to be explained by obstruction and increased resistance in the lungs.

I am sure that I do not know what the rales in the upper chest were from. It is possible that the patient had an infarct, but I do not see how we can say more than that his course was simply that of progressive heart failure with gradual narrowing of pulse pressure, eventual failure of the heart and death. So far as the diagnosis is concerned, I can go no farther than to say he had hypertensive and coronary heart disease, that he had congestive failure, that he may or may not have had an acute episode of coronary thrombosis,—although I would be willing to bet against it,—and that he had some obstruction or increased resistance in his pulmonary circulation, the nature of which I can only guess. It may be due to multiple pulmonary emboli or it may represent metastatic malignancy. I do not think he had any marked degree of nephritis.

Dr. Donald S. King: May I ask if there is such an entity as cardiopneumofibrosis?

Dr. George W. Holmes: I am sorry that you brought that up. Years ago I wrote a paper on the subject and have regretted it ever since. I doubt if there is such a thing.

Dr. King: How about fibrosis at autopsy in this case?

Dr. Holmes: In some cases with long-standing passive congestion there may be a certain amount of fibrosis, but the term is a misnomer. The findings are probably due to passive congestion or to stagnation of blood in the lungs. We often see a picture like this, which disappears after the patient is put on digitalis. I do not think there is a true fibrosis except in rare cases, but Dr. Mallory can answer that better than I.

Dr. Hampton: If these are infarcts and not emboli, I am going to be disappointed.

A Physician: I would like to ask Dr. Hampton if there is any possibility of fluid in the pericardial cavity.

Dr. Hampton: Yes, it is possible, but we could not make a diagnosis without fluoroscopy.

A Physician: It is significant that he had a cough all his life. I think that we would have to carry into the differential diagnosis the possibility of tuberculous pericarditis with emboli coming at the end.

Dr. Hampton: He has a scarred upper lobe on the right, or what appears to be one; we think that he probably had tuberculosis at one time to explain that. We did not see any miliary process, and there are no cavities.

### Clinical Diagnoses

Arteriosclerotic heart disease.
Pulmonary infarction.
Bronchopneumonia.

### Dr. Alfred O. Ludwig's Diagnoses

Hypertensive and coronary heart disease.
Congestive failure.
Multiple pulmonary emboli?
Lymphatic malignant metastases of the lung?

### Anatomic Diagnoses

Hypertrophy of the heart, hypertensive type.
Arteriosclerosis: coronary, marked; aortic, marked, with aneurysm.
Infarct of the heart, old.
Pulmonary emboli.
Pulmonary infarcts.
Thrombosis of the popliteal and the posterior tibial veins of the left leg.

### Pathological Discussion

Dr. Tracy B. Mallory: The postmortem showed an enlarged, hypertensive heart as prophesied, with a very marked grade of coronary disease. All branches of both coronaries were narrowed, but at the time of autopsy no one of them was completely occluded. I think we must assume that in the past one of them had been occluded and became recanalized, because there was an old, completely healed infarct at the apex. It must have been months, and probably years, old. There was no fresh infarction. The only thing found to explain any of the symptoms of the last month of his life was a series of thrombi in the lungs, of various ages and various degrees of adherence, with secondary infarcts of different sizes scattered throughout all five lobes.

Dr. Hampton: The scarring was due to infarction instead of tuberculosis?

Dr. Mallory: Yes. He had one other totally unsuspected and, as it turned out, unimportant finding, though it might easily have caused trouble if he had lived longer. This was an aneurysm of the abdominal aorta, just above the bifurcation, which was apparently arteriosclerotic in origin. The aorta at this point was definitely dilated, and the intima was shaggy and covered with clots which might easily have broken loose and produced emboli that would have occluded the leg arteries.

A Physician: Did he have thrombosis of the veins in his leg?

Dr. Mallory: There were thrombi in the deep veins of the leg, which were unquestionably the source of his pulmonary emboli since no thrombi were present in the cavities of the right side of the heart.

## CASE 23162

### Presentation of Case

A 16 year old native schoolboy was admitted complaining of inability to open his jaws.

The patient stated that he was well until 10 days before entry, when he injured his right hip while playing football. During the succeeding 2 days his right leg above the knee became painful and stiff. Eight days before entry he developed stiffness and pain in the left shoulder, profuse perspiration and general malaise. There were no chills. Two days before coming to the hospital he found it difficult to open his mouth and observed bilateral swelling and tenderness in the temporomandibular regions. At the same time there were stiffness of the neck and painful swelling of the right ankle. He became definitely feverish and shortly afterward developed pain and redness in the region of the right testicle. The day before admission there was pain in the right knee, and he was unable to open his mouth more than 1 or 2 centimeters. On the day of entry he developed a sore throat, slight cough and pain in the right lower chest on deep inspiration. X-ray examination of the right leg and shoulder taken by a physician were said to have been negative. History of exposure to venereal disease was emphatically denied.

Physical examination showed a well-developed and nourished boy lying flat in bed complaining of pain in the right hip, knee, ankle and left shoulder. The skin was hot and flushed, and over the arms, legs and chest were rare, small, slightly elevated, pink spots. There was definite ptosis of the left lid, and he was only able to raise the lid with effort. The right palpebral fissure was wider than the left, and there was slight internal strabismus. The neck was stiff, and the patient was unable to open his mouth more than 1 centimeter. The heart was not enlarged. There was a soft, systolic murmur heard over the precordium, which was loudest at the apex. The blood pressure was 120/80. At the right base posteriorly and anteriorly the breath sounds were slightly diminished, and occasional crepitant rales were audible. The remainder of the chest was negative. There was slightly increased resistance to palpation in the right flank, and tenderness was elicited on the right side. Examination of the genitalia showed a rather thin and watery urethral discharge. The right testis was red, swollen and tender, and the epididymis was thickened. There were periarticular warmth, redness and tenderness over both temporomandibular joints. Similar signs were noted over the left shoulder and the right hip, knee and ankle. A rectal examination was negative.

The temperature was 105°F., the pulse 135. The respirations were 30.

Examination of the urine showed a specific gravity of 1.022 with a slight trace of albumin. The sediment contained 100 white blood cells and a rare red blood cell per high power field, but was otherwise negative. Following prostatic massage a urethral smear demonstrated gram-negative intracellular diplococci on one occasion only. The blood showed a red cell count of 5,100,000, 75 per cent hemoglobin. The white cell count was 23,000, 84 per cent polymorphonuclears. Examination of the stools was negative. Pneumococci, types I, II or III, could not be demonstrated in the sputum. The nonprotein nitrogen of the blood was 28 milligrams per cent, and the uric acid was 3.5 milligrams per cent. Three blood cultures showed *Staphylococcus aureus.*

An x-ray film of the chest showed the left diaphragm to be obscured by a large heart, the enlargement being chiefly in the left ventricle. The aortic shadow appeared to be normal. The right diaphragm was slightly elevated and showed hazy mottling just above it. There was a slight angular area of this mottling at the apex, pointing into the hilus.

The patient's condition remained essentially unchanged, and his temperature ranged between 102 and 105°F. The pulse rose progressively to 160. Further examinations of the urethral smears showed pus cells but no organisms. An x-ray film of the chest on the third hospital day showed no significant change. The patient's condition became progressively worse, and he died on the fourth hospital day.

### Differential Diagnosis

Dr. John H. Talbott: This is the story of a 16 year old schoolboy who was sent to the hospital because of inability to open his jaws. I think the first thing most of us consider with such a history is lockjaw or tetanus. The symptoms began 8 days before admission to the hospital and 2 days after a football injury. The usual incubation period in tetanus is considerably longer than 2 days. The original hip injury was probably a hematoma in the muscle or a subperiosteal hematoma. No mention is made of an abrasion of the skin, and presumably no fracture of one of the bones of the hip was suspected. At the time of recurrence of symptoms in the right leg, the patient had involvement of other joints, with sweating and malaise. These are characteristic of an acute infection, and I think we must concentrate on this aspect of the case from now on.

Two days before coming to the hospital the patient was unable to open his mouth and had swelling and tenderness in the temporomandibular regions. At the same time there were involvement of other joints and stiffness of the neck. On the day of admission the patient had a cough and pain in his chest on deep inspira-

tion—symptoms which are suggestive of pleurisy accompanying either a pneumonia or an infarction.

The x-ray examination of the right leg and shoulder was said to be negative. We know that acute joints do not show evidence of involvement by x-ray until at least 2 or 3 weeks have elapsed after the first symptoms. The fact that the x-rays were negative does not rule out a process in the joints.

A history of exposure to venereal disease was apparently sought but not confirmed. The whole picture simulates, in many respects, an acute gonorrheal arthritis. I do not believe, however, that the gonococcus is the etiologic agent.

On physical examination the patient showed evidence of an acute infection, polyarthritis and meningeal irritation. On the skin there were small, slightly elevated, pink spots. Such spots are observed in septicemia, especially in meningococcus septicemia. The ptosis of the left lid was indicative of third nerve involvement. Strabismus is frequently an accompanying finding. We find that the neck was stiff. This means, I believe, that there was meningeal irritation as well as muscle or vertebral involvement. A soft systolic murmur was heard all over the precordium. We do not know whether this was a recent finding or a so-called functional murmur. If we knew that this murmur had not been present at a previous examination, we would be justified in making a tentative diagnosis of acute endocarditis in the presence of a septicemia. The breath sounds were diminished in the right lung base, and there were crepitant rales. This is consistent with either a small patch of bronchopneumonia or an infarct. The watery urethral discharge centers our attention again upon a possible generalized gonococcus infection. Against this is the negative prostatic examination. A prostatitis generally accompanies a gonorrheal infection, and the absence of this, I believe, is significant.

The patient was acutely ill, and only a few determinations were done in the hospital. The trace of albumin in the urine means to me nothing more than fever. The presence of gram-negative intracellular diplococci on one examination is difficult to evaluate. Again, if this were a fulminating gonococcus infection, I believe there should have been no difficulty in finding the organisms at repeated examinations. A red blood cell count of 5,000,000 suggests that the septicemia was of short duration. In typing the sputum they presumably were looking for a generalized pneumococcus infection to explain the whole picture. The uric acid concentration of 3.5 milligrams per cent is normal.

In the differential diagnosis of acute arthritides, a gouty polyarthritis should be considered. I do not believe that this is gout, and the normal uric acid is confirmatory evidence. In a large series of gouty and nongouty patients in this clinic, I have never observed a normal concentration of uric acid in any of the patients with proved gout.

Three blood cultures showed *Staphylococcus aureus*. *Staphylococcus albus* is frequently a contaminant in routine blood cultures, *Staphylococcus aureus* but rarely. Since blood cultures are taken in pairs, generally on different days, it is unlikely that at least two pairs were contaminated by the same organism. I believe, then, that the finding of staphylococci in the blood culture means staphylococcus bacteremia.

If the doctors had been seriously considering a gonococcus infection, they would certainly have used glucose broth for their culture medium, and organisms should have been grown with this technic. Other tests, which might have been done, but were not, because of the condition of the patient, are a complement fixation test and a lumbar puncture. The complement fixation test for the gonococcus may be positive within 10 days after the onset of joint symptoms but usually is not positive until the second or third week. We are, then, on the borderline of time to expect a positive complement fixation, and this might have contributed a little. A lumbar puncture would certainly have ruled in or out a meningococcus meningitis. At this stage of the disease, if the stiff neck had been caused by this organism, we would have found a large number of white cells in the spinal fluid and a lowering of the spinal fluid sugar. The spinal fluid findings in tetanus are usually normal.

I am at a loss to interpret the enlargement of the left heart by x-ray. On physical examination the heart was not enlarged. It is possible, but improbable, that an infarct near the hilus of the left lung produced this change, and equally unlikely is a septic infarct in the myocardium producing acute myocardial hypertrophy. The x-ray of the lungs showed an angular shadow characteristic of infarct in the right lung.

The patient's temperature ran a septic course, and he became progressively worse and died 4 days after admission. I believe this patient was suffering from a *Staphylococcus aureus* septicemia with emboli in the brain, meninges, skin, testicle and kidneys. The arthritis, also, was septic in origin. There were pulmonary infarcts, an endocarditis and possibly a myocardial infarct.

### Clinical Diagnoses

*Staphylococcus aureus* septicemia.
Gonorrheal urethritis and arthritis?

### Dr. John H. Talbott's Diagnoses

*Staphylococcus aureus* septicemia, with septic emboli.
Septic arthritis.
Pulmonary infarcts.
Acute bacterial endocarditis.
Myocardial infarct?

### Anatomic Diagnoses

*Staphylococcus aureus* septicemia.
Acute prostatitis, vesiculitis and epididymitis, *Staphylococcus aureus*.
Acute bacterial endocarditis, *Staphylococcus aureus*.
Pulmonary emboli.
Septic infarcts of the lungs.

### Pathological Discussion

Dr. Tracy B. Mallory: This patient showed at autopsy the characteristic findings of a widespread staphylococcus infection. The primary site of infection—perhaps it would be safer to say the point of first localization—was, as the history suggested, the genito-urinary tract. There was abscess formation in the prostate, and there were vesiculitis and epididymitis. The prostatic portion of the urethra was involved, but the infection had not extended back to the bladder, and the kidneys were entirely free. Smears and cultures from all these areas showed staphylococci but no gonococci, and I do not believe that gonococci were ever present. Staphylococci, especially when intracellular, can easily be decolorized if the gram stain is carelessly done, and it was never possible to check the house officer's original finding.

As Dr. Talbott suspected, an endocarditis had developed. It was, however, quite unusual in character. Whereas endocarditis usually appears upon a valve, and most often on a valve on the left side of the heart, the vegetations in this instance were in the right heart and involved, not the heart, but the apex of a papillary muscle and the corresponding chorda tendinea. This was probably the source of most, if not all, of the multiple emboli which were found in the lungs and which had produced multiple large infarcts. Some of the infarcts, as would be expected with *Staphylococcus aureus* infection, showed early evidence of abscess formation. We did not have permission to examine the head, but I have no doubt that metastatic abscesses must have been present, as Dr. Talbott predicted. The joints proved very disappointing; we opened several which were said to have been involved and could find nothing.

The New England
# Journal of Medicine

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## PRONTYLIN AND PRONTOSIL

THE true value of new therapeutic agents, such as prontylin and prontosil, as mentioned in a correspondent's letter in this issue of the *Journal* and as already commented upon editorially (this *Journal* **215:** 1311 [Dec. 31] 1936), can only be determined by exhaustive experimental and clinical trial in trained hands. These two new drugs are being tested extensively in many of the larger clinics in the United States. A few reliable reports have already appeared, and more will undoubtedly follow within a short period of time.

Although Massell's findings, in a limited number of cases, seem to indicate that prontylin has no effect on the recrudescence of rheumatic fever, on the duration of positive throat cultures for hemolytic streptococci, or on the course of active rheumatic fever or chorea, it must be acknowledged that a number of astonishing "cures" through the use of these drugs have been reported, both in the literature and by word of mouth; and there seems to be a certain amount of justification for their trial by the practitioner in *certain* cases. There is little else he can do for patients with *hemolytic* streptococci in their blood streams, unless he is so situated that the complicated technic of "immunotransfusion" can be properly carried out. The same is true for cases with a meningitis from infection with *hemolytic* streptococci. Furthermore, the physician can reasonably employ the drugs in cases of localized sepsis due to *hemolytic* streptococci, in order to prevent a generalized infection. No serious untoward effects following administration have been reported, but care should be taken to avoid overdosage. Their use in cases of sepsis of unknown etiology or of infection due to organisms other than hemolytic streptococci, unless no other therapeutic means are available and the outcome is utterly hopeless, is *contraindicated.*

The field of usefulness of prontylin and prontosil has yet to be defined, and *their employment by the practitioner should be confined to infections that have been proved, bacteriologically, to be due to Streptococcus hemolyticus.* If, by chance, the drugs are effective in other types of infection, let us hope that they will not fall into disrepute prematurely from ill-advised and illogical use.

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## DEAN BURWELL'S REPORT

DR. C. SIDNEY BURWELL, dean of the Harvard Medical School, reveals plans, in his annual report, to solve one of the pressing problems of modern medical training—the handicap that many brilliant students encounter in this field

where schooling is at once expensive and so difficult as to exclude outside work.

According to a release from the University News Office, special consideration is being given to the problem of able young graduates who, after a year or two of internship, are obliged to cut short their training and go into forms of activity that do not permit their full development, although they are capable of first-class productive work. By aiding these men with material grants, the development of the school, the training of leaders in medicine and the general advance of medical science would all be aided.

To further this plan the establishment of a number of fellowships ranging in value from $1,200 to $2,500 a year is proposed. These graduate fellowships, according to Dean Burwell, should not only be available to graduates of schools other than Harvard, but should be open also to suitable persons with Ph.D. degrees who would be accepted for training in one of the fundamental departments of the medical school.

A plan to care for the superior but needy college graduate who is considering medical education provides for the establishment of prize scholarships to relieve the brilliant student from the necessity of supporting himself by outside work. Scholarships of this sort, as have already been established in Harvard College and some of the graduate schools, would be adjusted to each individual's needs.

An additional problem that confronts the school in its endeavor to place medical scholarship on the highest possible level is the annual selection of entering men. An analysis of the records of men admitted to the school, compared with those of men rejected, has been undertaken in order to obtain the best possible type of student. In this effort the faculty seeks especially to avoid the admission of men temperamentally unfit for the pursuit of medicine and to include superior men whose preparation is unorthodox and therefore, at first sight, appears inadequate.

It is apparent from this report that the new dean at Harvard clearly understands the problems confronting medical education today, and we predict that the Harvard Medical School under his guidance will make satisfactory progress toward their solution.

## THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

MEIGS, JOE V. M.D. Harvard Medical School, 1919. F.A.C.S. Assistant visiting surgeon, Massachusetts General Hospital. Surgeon, Pondville Hospital. Associate surgeon, Collis P. Huntington Memorial Hospital. Instructor in surgery, Harvard Medical School. Address: 264 Beacon Street, Boston.

PARSONS, LANGDON. M.D. Harvard Medical School, 1927. F.A.C.S. Assistant surgeon, Massachusetts General and Pondville hospitals. Assistant in surgery, Harvard Medical School. Surgeon, Out Patient Department, Collis P. Huntington Memorial Hospital. Address: 264 Beacon Street, Boston. Their subject is "Granulosal Cell Tumors of the Ovary: A Report of Three Recent Cases." Page 681.

PALMER, ROBERT S. M.D. Harvard Medical School, 1925. Instructor in medicine, courses for graduates, Harvard Medical School. Assistant physician, Massachusetts General Hospital. Address: 330 Dartmouth Street, Boston. His subject is "The Factor of Mental Stress in Essential Hypertension." Page 689.

SCHUBE, PURCELL G. M.D. University of Cincinnati College of Medicine, 1929. Assistant superintendent, Boston State Hospital. Address: Boston State Hospital, Boston.

RITVO, MAX. M.D. Harvard Medical School, 1922. Visiting roentgenologist, Boston City Hospital. Assistant roentgenologist, Beth Israel Hospital. Assistant professor in roentgenology, Tufts College Medical School. Instructor in roentgenology, Harvard Medical School. Address: Boston State Hospital, Boston.

MYERSON, ABRAHAM. M.D. Tufts College Medical School, 1908. Professor of neurology, Tufts College Medical School. Clinical professor of psychiatry, Harvard Medical School. Visiting physician, Department of Nervous Diseases, Beth Israel Hospital. Consultant neurologist, Boston City Hospital. Director of research, Boston State Hospital. Address: Boston State Hospital, Boston.

LAMBERT, RUTH. A.B. Connecticut College for Women, 1935. Research technician in roentgenology, Boston State Hospital. Address: Boston State Hospital, Boston. Their subject is "Human Autonomic Pharmacology. IV. The Effect of Benzedrine Sulfate on the Gallbladder." Page 694.

BRAILEY, ALLEN G. M.D. Harvard Medical School, 1928. Assistant in medicine, Harvard Medical School. Address: 270 Commonwealth Avenue, Boston. His subject is "Treatment of Constipation." Page 697.

The Massachusetts Medical Society

## SECTION OF OBSTETRICS AND GYNECOLOGY*

R. S. Titus, M.D., *Chairman*, 472 Commonwealth Ave., Boston, Mass.
R. J. Heffernan, M.D., *Secretary*, 1101 Beacon St., Brookline, Mass.

### Case Histories

### No. 16. tubal pregnancy

Mrs. F. O., a white woman, aged 37 years, was seen in the office July 31, 1936. She complained of pain in the left lower quadrant of the abdomen of 3 days' duration and stated that the pain was a constant dull ache with attacks of sharp pain lasting a few minutes. There had been no nausea or vomiting. Her bowels moved daily without laxatives, and there was no increase in the pain during defecation. There was no frequency of, or burning during, micturition.

There was no family history of malignant disease, tuberculosis or diabetes. She had had tuberculosis of the lungs 10 years previously. An x-ray examination of the chest 1 year before was negative, however, and she had no symptoms of tuberculosis when seen. Her appendix and right tube had been removed because of inflammation in 1919. In 1923 labor was induced at 7 months for toxemia of pregnancy. There had been no other pregnancy. Menstruation began at 12 and had been normal and regular up to March, 1936, when she had a scanty period. Those in April and May were profuse, but the one starting on June 18 was a normal flow of 6 days. There had been no menstruation since that time. She had been staining off and on for 7 days before she was seen.

On physical examination, the patient was well developed and nourished. Her color was normal, but she was evidently having pain. Her temperature was normal. The head, neck, throat and teeth were negative. The chest was symmetrical, expansion was free and equal; resonance, fremitus and breath sounds were normal, and there were no adventitious sounds. The heart was not enlarged or displaced, and there were no murmurs. The cardiac rhythm was regular; the blood pressure was 120 systolic, 85 diastolic; and the pulse rate was 80 per minute. Some white fluid was squeezed from both nipples, but she stated that this phenomenon had been present for many years. The breasts were otherwise negative. There was tenderness across the lower abdomen, which was worse on the left, but there was no spasm. Vaginal examination revealed a good perineum, a negative cervix with a little blood coming from its canal and a normal-sized uterus in good position. On the left was a tender mass 8 to 10 centimeters in diameter. The rest of the pelvis was soft and not tender. A rectal examination added nothing.

It was thought that the patient might have an ectopic pregnancy, but that pelvic inflammation, tuberculous salpingitis, a bleeding corpus luteum and ovarian cyst must be considered. The lack of fever was against pelvic inflammation, and the soft pelvis was against a bleeding corpus luteum, which might occur at this time—the middle of the menstrual cycle. The apparent absence of blood in the posterior cul-de-sac was somewhat against tubal pregnancy.

She was sent home to stay in bed and to report if her pain increased. She was also instructed to save a morning specimen of urine for an Aschheim-Zondek test.

She was seen at 9 o'clock the next morning, when she said that the pain had increased in intensity during the night. There had been no nausea or vomiting, and her bowels had moved. She was still flowing a little.

The abdominal examination showed no change. The vaginal examination showed an appreciable enlargement of the mass on the left, with increased tenderness; the rest of the pelvis was negative.

The changes in the pain, the size of the mass and the tenderness were believed to be indications enough to warrant an immediate operation, which was performed.

Examination under anesthesia showed that the mass was somewhat movable, tense and firm, but not hard. A curettage of the uterine cavity was negative. The abdominal operation revealed an enlargement of the distal two thirds of the left tube, measuring 10 by 8 centimeters, which was apparently due to blood clot inside the tube; the fimbriated end was adherent to the left ovary. There were a little blood in the pelvis and a good many old adhesions involving the uterus, right ovary, intestine and omentum. A supravaginal hysterectomy, bilateral oophorectomy and left salpingectomy were done. The patient had a normal convalescence and was discharged on the sixteenth day after operation.

The pathological report was as follows: "Tubal pregnancy, left; secretory endometrium of early pregnancy with decidua; normal uterine wall; periovaritis, bilateral."

The Aschheim-Zondek test, which was started the morning of operation, was positive.

*Discussion.* This is a typical case of tubal pregnancy, which is somewhat confused by the past history of tuberculosis and the possibility of the symptoms being due to a bleeding corpus luteum, to ovarian cyst with a twisted pedicle or to inflammation.

*A series of selected case histories by members of the Section will be published weekly.

Comments and questions by subscribers are solicited and will be discussed by members of the Section.

The menstrual dysfunction of 4 months might go with tuberculous or pyogenic salpingitis, but the pain was too great for such conditions and the negative pelvis, except for the mass, was against them. The acute pain with a bleeding corpus luteum lasts only a few hours, as a rule. The staining off and on for a week is typical of ectopic pregnancy and not of ovarian cyst. No sensation of fluid in the cul-de-sac was found, because the pregnancy had not aborted from the tube.

The uterus and ovaries were removed in this particular case because there were so many adhesions in the pelvis. It was believed that, if they had been left in, she would have required another operation for pain from adhesions. It is not necessary to do this in the average case.

## ANNUAL MEETING

THE one hundred and fifty-sixth annual meeting of the Massachusetts Medical Society will be held in Boston at the Hotel Bradford, June 1, 2 and 3.

The Shattuck Lecture will be given Tuesday evening, June 1, by Dr. Henry D. Chadwick, Commissioner of Public Health of Massachusetts. His subject will be "The Diseases of the Inhabitants of the Commonwealth."

Dr. Charles G. Heyd, of New York City, president of the American Medical Association, will be the principal speaker at the annual dinner on Wednesday evening, June 2.

## ANNUAL MEETING OF AMERICAN MEDICAL ASSOCIATION

THE Massachusetts Medical Society has received from the officers of the American Medical Association the Official Call announcing that the eighty-eighth annual session of the American Medical Association will be held in Atlantic City, from Monday, June 7, to Friday, June 11.

The House of Delegates will convene on Monday, June 7, and the Scientific Assembly will open with the General Meeting on Tuesday, June 8, at 8:30 p. m.

The various sections of the Scientific Assembly will meet Wednesday, June 9, at 9 a. m. and 2 p. m., and subsequently according to their respective programs.

The Massachusetts Medical Society is informed that it is entitled to six delegates.

ALEXANDER S. BEGG, M.D., *Secretary,*
Massachusetts Medical Society.

# MISCELLANY

## ADDITION TO THE BOSTON DISPENSARY

On April 8 the administrative committee of the Boston Dispensary announced the gift of nearly $500,000 from William Bingham, 2nd, of Bethel, Maine, for the construction and equipment of a 100-bed hospital. The new unit will be called the Joseph H. Pratt Diagnostic Hospital in honor of Dr. Pratt, who has been so successful in the past 10 years in promoting the New England Medical Center—an organization for training family physicians and for assisting them in their diagnostic problems. The donor has further agreed to finance any deficits arising from the operation of the new unit.

The building will have a frontage of 140 feet on Bennet Street, opposite the Boston Dispensary, and will be connected with the latter by a tunnel. The facilities of the hospital will be used for undergraduate and graduate teaching and for medical research in connection with Tufts College Medical School. Construction will begin relatively soon, and the building is expected to be ready for occupancy early next year.

## FIFTH INTERNATIONAL CONGRESS OF RADIOLOGY

One of the most outstanding scientific events ever held in the United States has been set for Chicago this September, when the Fifth International Congress of Radiology convenes. It will be the first time that the world leaders in the medical and scientific development field of x-ray and radium have met in America, according to Dr. Arthur C. Christie, Washington, D. C., president of the Congress. The dates are September 13 to 17, inclusive, and the meeting place is the Palmer House.

At least 500 distinguished delegates and guests from a score of European countries as well as physicians from Mexico, Canada and Central and South America are expected to attend, with more than 2,000 other delegates and visitors from all parts of the United States.

The annual medical conventions of the leading radiologic bodies of this country will be merged with the international congress. These include the American Roentgen Ray Society, the American College of Radiology, the Radiological Society of North America and the American Radium Society.

The First International Congress of Radiology convened in London in 1925. Meetings are held every three years. The physicians and physicists met in Stockholm in 1928, in Paris in 1931 (where they paid tribute to the then living Madame Curie, co-discoverer of radium) and in Zurich in 1934.

Leaders in other branches of medicine will participate in the Congress, as Dr. Christie points out that "The Unity of Medicine" will be the theme of the entire Congress. "These international congresses seek to maintain a continuity of program over the years, and, in consequence, such vital subjects to the radiologist, and to the general public, as diagnosis and treatment of cancer and many other diseases and teaching and training in radiology will be on the agenda of this Congress as well as at former meetings.

"Radiology is an important branch of medicine

and is, indeed, part of the entire tree, and not merely a specialty as it was once regarded," added Dr. Christie.

More than 250 scientific papers will be read at the five-day meeting. These will be delivered in each lecturer's own language and will be automatically flashed on screens in English, German and French as the papers are read.

What will probably be the greatest scientific and technical exhibit in the history of a radiologic congress will be assembled by physicians, physicists and manufacturers of such equipment in conjunction with the Congress.

The general secretary of the Congress, Dr. Benjamin H. Orndoff, is in charge of headquarters at 2561 North Clark Street, Chicago, Ill. Honorary vice-presidents are Dr. George E. Pfahler, of Philadelphia; Dr. James Ewing, of New York; and Dr. William D. Coolidge of Rochester, N. Y. On the International Executive Committee are Dr. Arthur C. Christie, of Washington, D. C., chairman; Dr. C. Thurstan Holland, of Liverpool; Dr. Gosta Forssell, of Stockholm; Dr. Antoine Beclere, of Paris; Dr. Hans R. Schinz, of Zurich; Dr. Karl Frik, of Berlin; Dr. Mario Ponzio, of Florence; Dr. Tamotsu Watanabe, of Osaka, Japan; Dr. Heliodoro Tellez-Plasencia, of Santander, Spain; and Dr. Gottwald Schwarz, of Vienna.

## FIRST U.S.P. SUPPLEMENT DELAYED

There has been a slight delay in the issuance of the first U.S.P. supplement, due to changes in plans for the binding. It was originally proposed that the supplement should be issued with a stout paper cover and that this would be enclosed in a strong spring-back binder capable of also holding such future supplements as would be issued.

Now, however, to make the supplement less costly it has been decided to offer it without the spring binder, although the binder will still be available for those who desire it. The purpose of the spring binder has been to keep all supplements together and in such form that they may stand on the shelf by the original "Pharmacopoeia," or be serviceable in the laboratory. With this change in plans the individual supplement will be bound in a more substantial, but flexible, cover. The proper development of this feature has taken a longer time than was expected.

The supplement soon to be issued will be known as the "First Supplement to the Pharmacopoeia of the United States, Eleventh Decennial Revision." It may not be necessary to issue supplements annually, but these will be published whenever the number of new interim revision changes justifies their publication. The delay in the release of the first supplement will no doubt necessitate an advance in the date when the new standards are to become official.

Orders for the "First U.S.P. XI Supplement" should be sent to The Mack Printing Company, Easton, Pa., or to any of the regular distributing agencies for the "Pharmacopoeia." The price will be $1.00.

## A FREE SET OF BOOKS

"You have been selected to receive some free books with the compliments of the publisher." Thus a free offer may come to you by way of a form letter or personal solicitation. Usually you are told that because of your "prominence", or for "advertising purposes", you will receive a set of "free" books.

But, the hook in this scheme is often baited with the supplementary service required to keep the books up-to-date. For this you usually pay a price sufficient to cover the cost of both the "free" offer and the service. Incidentally, unless you buy, you do not get the "free" books.—*Boston Better Business Bureau.*

## MAINE NEWS

Remarkable success throughout the State marked the National Cancer Week drive put on by the Women's Field Army auxiliary of the American Society for the Control of Cancer. Mrs. William Holt, of Portland, the state commander, showed splendid energy and efficiency in the organization of her groups and the selection of her lieutenants. All of the large cities and many of the smaller ones were visited by Mrs. Holt, and local committees were formed. Contributions have come in in sufficient amount to indicate an enthusiastic response to this drive.

A $25,000 fund, sought by the Maine Women's Field Army, will be known as the Dr. Joseph W. Scannell Fund. Dr. Scannell, who died recently in Lewiston, had devoted much of his time to the study and cure of cancer.

With the cooperation of the physicians of the State a cancer talk was given during National Cancer Week before every nurse in training in every hospital in the State, all service clubs, women's clubs and state granges, besides the smaller church and fraternal groups.

An effort is being made to have all county medical societies follow the lead of Kennebec County, which has a five minute talk on some phase of the cancer problem at every county meeting during the year, this being an effort to keep the subject alive in the mind of the general practitioner.

The eighty-fifth annual session of the Maine Medical Association will be held at the Belgrade Hotel, Belgrade Lakes, Maine, June 20, 21 and 22.

## NEGRO HOSPITALS

Plans for the establishment of Negro hospitals in 90 American cities having a Negro population of 10,000 or more were discussed at a recent meeting at the Peter Bent Brigham Hospital, which was presided over by Dr. Henry A. Christian. The principal speaker was Rev. Dr. Amos H. Carnegie, who has traveled all over the United States in behalf of the movement.

The proposed hospitals would provide adequate facilities for the care of the Negro population and would furnish opportunities for the proper training of Negro physicians and nurses. It is planned to finance the scheme by donations of 1 cent a week for 20 years from the 13,000,000 Negroes in this country. Such a plan, if successful, would result in a fund of over $100,000,000.

## CORRESPONDENCE

### PRONTYLIN AND PRONTOSIL

March 23, 1937.

Editor, *New England Journal of Medicine*,

After reading the article on prontylin by Dr. B. F. Massell (this *Journal* 216:487 [Mar. 18] 1937) it seems to me that the makers of this already famous panacea for hemolytic streptococcus infections have outdone themselves. Despite the fact that doctors have long sought such a remedy, a claim such as this one should be thoroughly tried by our research workers before it is even tested by our hospitals.

There is no question about the overenthusiasm of the medical profession for "sure cure" remedies. I do not see how this remedy gained such quick recognition, but it goes to show that doctors are just as gullible to exploitation of cures as the laity. In the future I shall consign all ultrascientific literature to the wastebasket, and I hope that a great number of other physicians will do likewise.

PAUL NETTLE, M.D.

282 South Main Street,
Bradford, Mass.

April 17, 1937.

Editor, *New England Journal of Medicine*,

I am submitting a short case report of a severe neutropenia occurring during the use of prontylin. As this drug is now being quite extensively used it was considered that this report might be of sufficient importance for publication.

M. M., female, aged 54, had a subacute bacterial endocarditis of about 5 months' duration. Her blood culture was positive for *Streptococcus viridans;* her white cell count was 26,000 and red count 3,200,000 per cu. mm. of blood. On February 14, 1937, she was started on 15 grains of prontylin daily. This was increased to 20 grains daily on February 18, which dosage was continued until March 21, when she discontinued its use on account of nausea and vomiting. On March 1 her white count was 17,000, and the blood culture still positive. On March 12, her white count was 21,000. On March 24, five weeks after beginning prontylin treatment, her white count had fallen to 400, and no neutrophils were found on stained smears. Her red count was 3,580,000, and platelets were present in large numbers. She was extremely weak. On March 25, the white count had risen to 1,600, her blood culture was strongly positive for *Streptococcus viridans*, and there was an extensive gangrenous infection of the mouth and pharynx. She died on this day. As no other drugs were administered with the prontylin, and so far as could be ascertained she had taken no other drug, it was considered that the neutropenia was due to the prontylin.

Very truly yours,

HERBERT E. PLUMER, M.D.

899 Beacon Street,
Boston.

### IODINE AS A WOUND ANTISEPTIC

April 2, 1937.

Editor, *The New England Journal of Medicine*,

I was a little perturbed by the editorial which I read in the March 25 issue of *The New England Journal of Medicine* on "Iodine as a Wound Antiseptic."

I feel that the day of antiseptics is slowly coming to an end, especially in reference to the treatment of fresh wounds, either surgical or traumatic. It makes me shiver to see somebody apply iodine or some other antiseptic to a freshly made wound, as there is no question that any antiseptic is bound to kill as many or more living cells as it does bacteria. The public is still antiseptic-minded and I think it is up to the medical profession to correct this attitude. I feel an editorial denouncing antiseptics in the treatment of wounds would be more to the point than recommending them for this use. I am fully in accord with the principles laid down by Dr. Mont Reid in his address to the Massachusetts Medical Society, which was published in *The New England Journal of Medicine* (215:753 [Oct.] 1936). The only place that I consider an antiseptic such as iodine of value is in the preparation of intact skin prior to an operation. Even here I do not feel entirely sure that it is necessary. I am referring all my students to Dr. Reid's article, and every opportunity I have I try to enlighten people on the fallacy of using antiseptics.

Very truly yours,

R. R. LINTON, M.D.

Massachusetts General Hospital,
Boston.

EDITOR'S COMMENT: The editorial and the original article to which it referred distinctly state that antiseptics as applied to "minor cuts, wounds and abrasions" were the ones considered. As the correspondent states, the public is "antiseptic-minded," and one of the evident objects of both the article and the editorial was an attempt to point out to the physician the relative ineffectiveness of the proprietary antiseptics, in the hope that he might have some influence on lay usage. If the public *must* use antiseptics, why not have them use something that is effective?

Although the experimental work given in the original article showed that iodine is more toxic for body cells than for staphylococci, one is led to be-

lieve that cell necrosis in minor wounds, cuts and abrasions would not be a particularly serious matter, particularly if a dilute (0.5 to 1.0 per cent) iodine solution were used.

April 10, 1937.

Editor, *New England Journal of Medicine,*

Your editorial "Iodine as a Wound Antiseptic" was timely and excellent. Most clean wounds become infected as the result of faulty operative technic and it is unfortunate that so many unnecessary preparations are being used by the medical profession and hospitals.

I trust a large number of your readers will grasp the importance of this article and assist in simplifying and making more efficient operative procedures.

Very truly yours,
R. D. MARGESON, M.D.

520 Commonwealth Avenue,
Boston.

## RURAL NEW ENGLAND

April 12, 1937.

Editor, *New England Journal of Medicine,*

The enclosed manuscript is obviously worthless from a scientific standpoint, but it might be used as an amusing explanation of the origin of the beliefs still prevalent even within a few years in rural New England.

I may add that the tale is quite unvarnished. It all happened exactly as related.

Yours truly,
RAYMOND R. ROOT, M.D.

7 Pleasant Street,
Georgetown, Mass.

* * * * * *

### THE BIRTH OF TRADITION

The winter sun, haloed as its rays penetrated the film of steam on the windowpanes, had routed imperceptibly the yellow light of the small kerosene lamp. It was long after daylight when one of the weary watchers realized that its usefulness was ended, and blew it out. . . . With startling suddenness a cat of nondescript color leaped upon the sill outside the window. Its night's adventures over, it cried twice for admission without result, then settled down on its sunny shelf. . . . The solitary geranium inside the window, which in the kindlier light of the lamp had seemed not wholly without possibilities, was now revealed in all its rank, yellowish growth, fit product of a chain store tomato can.

"Don't you think it is time that afterbirth came, Doctor?" Mrs. Paine asked the question with a slight querulousness in her tone. In spite of her nearly eighty years, there was still in her erect, bony frame a vestige of professional authority based on many, many years of officiating, with or without medical direction, at such occasions.

The doctor did not answer at once. She had asked the same question many times in the past half-hour, and it was getting a little tiresome. There was no reason for haste, now. A slight movement of an old piece of blanket on a sofa, accompanied by a feeble cry, proved that the principal object of the night's vigil had been successfully accomplished.

"I imagine it will come along most any time now," he finally replied.

Temporarily satisfied, the old neighborhood nurse rearranged the blanket over the baby, then returned to her position leaning over the foot of the bed. She wore a dress of some faded, black material, whose skirt swept the floor. But her apron was fresh and white. Her thin, gray hair was brushed straight back from the gaunt face, whose hawklike nose and recurving chin nearly met. Far down the bridge of the nose balanced a pair of steel-bowed spectacles. The doctor thought that she probably resembled the legendary witch more closely than had many of the unfortunates hanged in Salem. . . . There was little or nothing for her to do now, but wait. The washing of the baby had better not be begun until this other business was finished.

At the head of the bed, bending over his wife, stood Mr. Reade, short, preposterously cross-eyed and almost completely bald. Although Mrs. Reade was perfectly calm and comfortable, he fanned her vigorously with a folded farm journal, at intervals straightening up to direct the breeze at his own flushed face. It was evident that a night of impending paternity had taken its toll of his nervous strength.

This was Mrs. Reade's first baby. She was very young, very unintelligent, obviously a slack housekeeper; but the consummation of motherhood had given her that transient aura that seems to lend a fleeting loveliness to even the least attractive at this moment of creation.

The doctor sat beside the bed, one gloved hand obscured in the folds of a sterile sheet on the mother's abdomen. He could easily keep informed of the contractions of the uterus while marveling at the gilt-framed chromo, sole work of art in this transformed parlor. It was not the super-Alpine height of the mountains depicted by the artist that held his attention, nor the mysterious, subterranean disappearance of the torrent falling over the cliff in the background. The feature that fascinated him was a white cottage in the foreground, with fences extending from each side of the front door straight to the brink of a precipice of terrifying depth. Should be easy to rent, he thought, after one of these stock-market crashes.

"Doctor, don't you think that if Mrs. Reade blew on the back of her hand it would make it come?" Mrs. Paine had remained silent as long as possible.

"No, I don't believe it would," replied the doctor. He knew from the condition of the uterus that the placenta had not become detached.

"Well, your father told me about that way more than fifty years ago, and I've seen it work a good many times."

"I know, but times have changed in fifty years, Mrs. Paine."

Silence for a few minutes. Then, "Well, do you mind if she tries it, Doctor?"

"No, go ahead if you want to, but it won't do any good."

Delighted to be in action again, Mrs. Paine instructed the willing patient in the exact manner of clasping her hands and how to blow on the back of one of them. All was ready; the patient blew hard and long; repeated the performance—all without result.

"You see, Mrs. Paine, it's just as I told you. Times have changed," said the doctor.

Somewhat chagrined, she replied, "Well, I've seen it work, over and over again. I don't see why it doesn't now."

While she was speaking, the doctor felt the uterus rise under his hand. He knew that he could probably express the placenta easily now.

"But I'll tell you what will bring it, every time," he said.

"What's that?" she asked.

"If the mother will blow on a bald head, the afterbirth will come every time. Never knew it to fail."

"You don't say so! I never heard of that," she said in an astonished voice.

"Well, it will," he replied.

"Why, look, Mr. Reade is baldheaded!" she cried.

"That's so, you're right," said the doctor, apparently surprised in his turn.

"Do you suppose it would work with him?" she asked.

"Don't see why not, he's certainly bald enough."

"Can we try it?" was the next question.

"Surely, if he's willing," agreed the doctor.

The new father proved more than willing to make an asset of what he had always considered a liability. He was carefully instructed as to the exact position to place his head for easiest reach of the patient; while Mrs. Paine nearly lost her glasses trying to miss none of the technic at the head of the bed, which might be so helpful to her upon some future occasion, and at the same time to watch for results from this maneuver so new to her.

At last all was ready, and the patient blew directly at the bald pate. At the same time, with a motion imperceptible to all, the doctor's hidden hand pressed down firmly on the uterus.

Never was therapeutic effort more promptly rewarded. Cause and effect were here synchronous. And out popped Mrs. Paine's eyes, until it seemed they might push off her spectacles completely.

"Why, Doctor! I never saw anything like that in all my life," she exclaimed.

"Well, Mrs. Paine, you see now that we've made some progress in baby cases since you and my father started out nearly sixty years ago."

"Oh, if I'd only known about that all these years," she said regretfully.

"Well, you don't always find anyone as bald as Mr. Reade," the doctor consoled her, as he began to pick up his instruments.

## IMMUNIZATION AGAINST DIPHTHERIA

The Commonwealth of Massachusetts
Department of Public Health

April 1, 1937.

Editor, *New England Journal of Medicine*,

In a recent publication distributed to all physicians by one of the prominent drug companies, there appears an article regarding the one-dose alum-precipitated toxoid. The import of this article is that this material should be used in preference to all other immunizing agents and that there are no conditions under which the use of this product may be contraindicated. This article leaves a very definite impression that the one-dose alum-precipitated toxoid is an immunizing agent superior in all respects to other similar products. Inasmuch as the Department of Public Health does not distribute the alum-precipitated toxoid and has consistently recommended against its use, it seems desirable that the Department should set forth at this time the reasons which underlie its objections to immunization through a single dose of alum-precipitated toxoid.

This material was advanced as an agent which could be used in a single injection. The literature, after its introduction, was quickly filled with articles showing that 95 to 100 per cent of the children given a single dose of this material were Schick negative one to three months afterward. This would not, however, give any assurance that the immunity so produced was lasting, inasmuch as the work of Glenny has shown that with any such immunizing agent the circulating antitoxin rapidly rises to a peak and then declines to a level substantially below this maximum. The Department was, therefore, not convinced that these high percentages of immediate protection give any guarantee of a lasting immunity.

That these suspicions were well founded has been indicated by subsequent results. Fraser and McKinnon in Toronto have shown that the circulating antitoxin in those immunized with the one-dose toxoid falls within a year to so low a level that less than one-half of those so injected are ultimately immune. In the August, 1936, issue of the *American Journal of Public Health*, Pansing and Shaffer, working in Ohio, showed that, of 549 children Schick negative one to six months after alum toxoid, 58 per cent had reverted to Schick positive at the end of two years. The February 6, 1937, issue of the *Weekly Bulletin* of the California State Department of Public Health stated that, of 293 children immunized with one-dose alum toxoid, 30 per cent were still Schick positive six months later. There is rapidly accumulating in the English literature, largely in the *Lancet* and the *British Medical Journal*, overwhelming evidence that the protection from the one-dose alum-precipitated toxoid is not adequate. As a result, the one-dose method has been virtually abandoned in England, and studies are going on as to the value of two injections of the alum toxoid.

In addition to these data, which raise much doubt as to the permanence of the immunity from the alum-precipitated toxoid, it is interesting to note the experience of New York City, which early indorsed the alum-precipitated toxoid and recommended its use for preschool children. Later, in May, 1936, the *Quarterly Bulletin* of that Department stated, ". . . It is true, Park says, that either one or two injections will apparently immunize about 95 per cent of the children treated with toxoid (ordinary toxoid in solution or toxoid in the form of an alum precipitate), but he finds that after only a single injection about half of the children are again Schick positive at the end of one year, whereas after two injections most of the children are still immune." Later, in August, 1936, the *Bulletin* of this Department contains the following statement: "Evidence is accumulating that immunization of children under nine months of age is less effective and probably less permanent than at nine months; further, that the one injection of alum toxoid does not confer as high a degree of immunity as two injections of plain toxoid. In the immunization made in the various stations of the Department of Health the use of alum toxoid has been discontinued. We now advocate immunization of children at nine months of age and the administration of two doses of plain toxoid." Thus, we find the New York City Health Department, after an experience with alum-precipitated toxoid, has decided to go back to ordinary toxoid. Other health departments have had similar experiences.

The second reason that the Department of Public Health did not indorse or distribute the alum-precipitated toxoid was the fact that there was still much that had to be learned as to the manufacture of the material to make certain that it would not produce sterile abscesses in a certain percentage of the cases. Although enough has been learned to reduce the incidence of these, it is still not possible to produce uniformly a product which is devoid of the risk of occasional sterile abscesses.

In opposing the use of alum-precipitated toxoid, the Department has at the same time strongly recommended the use of ordinary toxoid in three injections at three-week intervals. In many parts of the country, attempts have been made to immunize through the use of but two injections at intervals of a month. While unquestionably a very substantial number of children can be so protected, there is still not sufficient evidence to indicate that this type of protection is as satisfactory as that which comes from three injections. In a recent report from the Detroit City Health Department, the statement is made that 40 per cent of the children who had diphtheria in 1935 had presumably been immunized at a prior date. The immunizing agent used in Detroit has been two doses of ordinary toxoid and, after January 1, 1935, one dose alum toxoid as an alternative. Thus, in this series of 220 cases, there had been 40 per cent failures with these short-cut, immunization methods. Beginning July 1, 1935, the Massachusetts Department of Public Health began obtaining individual histories on all cases of diphtheria. When in September, 1936, a study was made of these, there were 220 case records in which the data were adequate for analysis. Of these, only 19, or 9 per cent, had presumably been immunized. In 8 of these 19 cases, the diagnosis was based entirely on clinical findings in spite of consistently negative cultural findings, so that there might have been reasonable doubt as to the accuracy of the diagnosis. Furthermore, with respect to the remaining 11, there was some doubt as to the actual immunization of 3 or 4, as the families claimed that the child had been immunized by physicians who had neither records nor recollection of having given such injections. Even assuming, however, that all of these 19 were authentic failures, the records showed but 9 per cent failures with the use of the more conservative three-doses of toxin-antitoxin or toxoid, as compared with 40 per cent failures in Detroit where the short cuts of two doses of toxoid or one dose of alum-precipitated toxoid were used.

In view of these data and many additional findings too numerous to list in this communication, the Department of Public Health feels justified in continuing to recommend against the use of alum-precipitated toxoid and, furthermore, to continue to recommend that, when immunization work is being done, three injections of toxoid should be given, preferably at three-week intervals. It is the feeling of the Department that if immunization is worth doing at all, it is worth doing well. The burden of proof rests upon those who maintain that the protection from these short cuts is as good or as lasting as from the conservative methods which have yielded such striking results in the reduction of diphtheria in Massachusetts.

Very truly yours,

HENRY D. CHADWICK, M.D.,
*Commissioner of Public Health.*

State House,
Boston.

## RECENT DEATHS

**MINITER**—FRANCIS GABRIEL MINITER, M.D., of 13 Sparhawk Street, Brighton, died at the Carney Hospital on April 10. He was in the fifty-fourth year of his life.

A graduate of the Tufts College Medical School, Dr. Miniter was particularly interested in otology, laryngology and rhinology. He was a member of the Massachusetts Medical Society, the American Academy of Ophthalmology and Oto-Laryngology and the New England Otological and Laryngological Society.

**WEISER**—WALTER R. WEISER, M.D., of Daytona Beach, Florida, died at his home on April 13. He was in the sixty-eighth year of his life.

A native of York, Pennsylvania, Dr. Weiser re-

ceived his medical degree from the University of Pennsylvania School of Medicine in 1892. From 1894 to 1917 he practiced medicine in Springfield and was chief surgeon of the Massachusetts State Hospital for eighteen years. He served in the medical corps of the United States Army during the World War. He came to Florida after his retirement from active practice in 1922. He was a former member of the Massachusetts Medical Society.

His widow and one son survive him.

## REPORTS OF MEETINGS

### SPECIAL LECTURES IN ENDOCRINOLOGY

Dr. Gordon C. Ring presented two of the special lectures in endocrinology at the Harvard Medical School on February 23 and 25, 1937, on the subject, "Endocrine Factors Concerned with Diabetes." Dr. Ring pointed out several striking similarities between the diabetic individual and the normal individual that is subjected to abnormal conditions. Thus, when a normal, well-nourished subject has fasted for several days, a marked ketosis develops, and the respiratory quotient falls to levels approximating those seen in diabetic patients. As the fat stores of the body are depleted, the ketosis diminishes, the respiratory quotient rises to a more normal level, and there is an increase in the nitrogen excretion. Undernourished individuals subjected to fasting do not develop ketosis, however. The ketosis of diabetic animals is observed to diminish or to disappear as the fat stores are depleted, and the low respiratory quotients present during the period of ketosis rise to within the normal range as undernutrition progresses. The low respiratory quotient of diabetics must not be interpreted as signifying an inability on the part of the animal to burn carbohydrates. Fasting nondiabetic individuals show a low sugar tolerance, and frequently glycosuria, after the ingestion of carbohydrate. A similar phenomenon is observed in well-nourished animals or human beings who have been maintained on a high fat diet for several days. The blood sugar curve in such individuals may simulate that of mild diabetes, indicating that a high fat intake impedes normal carbohydrate combustion, a supposition that is further strengthened by the fact that insulin is less efficient in lowering the blood sugar in persons on a high fat intake than it is in those on high carbohydrate diets.

Although it is known that the administration of insulin to a diabetic patient causes a lowering of the blood sugar, a disappearance of ketosis, a storage of glycogen in the liver, a decrease in the nitrogen excretion and an elevation in the respiratory quotient, it is still unknown what role insulin actually plays in the metabolic processes. The demonstration that the respiratory quotient of depancreatized, pituitarectomized animals is approximately normal indicates that insulin is not essential for the metabolism of carbohydrate. The liver glycogen in such animals has been found to be elevated rather than lowered, and in a heart-lung-liver preparation insulin actually causes a decrease in liver glycogen and a rise in the blood sugar.

A study of the blood sugar levels in arterial and venous bloods has shown that, as the degree of diabetes increases in severity, the difference in the two levels decreases, until in extreme diabetes there is no difference between the two values, indicating that the tissues have removed none of the sugar from the blood. Using an isolated heart, Evans demonstrated that insulin increased the utilization of sugar fivefold. These two findings would suggest that insulin is intimately connected with the removal and usage of glycogen by muscular tissue.

The depancreatized animal has been found to differ from the human diabetic in regard to the blood fat, which is elevated in the human being, but reduced in the experimental animal. The blood fat is elevated in such animals when they are fed whole pancreas, and their survival period is greatly prolonged by this procedure. Diabetic animals on normal diets develop a marked accumulation of fat in their livers, which disappears if they are fed raw pancreas. Banting and Best discovered that lecithin and choline were also satisfactory in preventing fatty infiltration of the liver, proving that it was not the external secretion of the pancreas which was effective in the raw pancreas. Dragstedt has isolated a second hormone from the pancreas. The evidence for its existence may be summarized as follows: (1) if the pancreatic duct is externalized to prevent the secretion of pancreatic juices into the gastrointestinal tract, no fatty infiltration of the liver occurs; (2) in the diabetic animal the ingestion of pancreatic juices does not influence the development of fatty infiltration; (3) ingestion of raw pancreas in amounts too small to contain enough choline to be effective prevents fatty infiltration, while ingestion of brain tissue (rich in choline) does not prevent such infiltration; and, finally, (4) pancreatic extracts containing only inconsiderable amounts of choline prevent fatty infiltration when fed or injected. It is quite probable that the human diabetic does not suffer from a deficiency of this hormone.

The metabolism of fat is markedly disturbed in diabetes, as is evidenced by the previously described high blood fat and fatty infiltration of the liver, by the increase in the specific dynamic action of fats in diabetics, and by the fact that the body fats are more highly saturated in diabetics than in nondiabetics. Insulin causes some desaturation of these fats.

The question of the relation of the thyroid gland to diabetes has been raised because of the elevated basal metabolic rate observed in diabetes, and because the sugar tolerance curve of hyperthyroid patients is almost indistinguishable from that of patients with mild diabetes. Dr. Ring believes that the latter finding can be accounted for by the marked depletion of liver glycogen which occurs in the

hyperthyroid state. The aggravation of diabetes produced by hyperthyroidism and its temporary alleviation by thyroidectomy can be accounted for by the variations produced in the metabolic rates. There is no need to postulate a specific role for the thyroid in diabetes.

In spite of the elevation of blood sugar produced by large doses of adrenalin and despite the glycosuria occurring after prolonged hyperactivity of the sympathetic nervous system, investigations have indicated that the adrenal medulla and its secretions are not involved in experimental diabetes.

Lactose and galactose relieve acidosis more readily than glucose, and liver glycogen formed from these substances is more easily liberated than that formed from glucose. There is some evidence that the presence of adequate glycogen stores in the liver prevents the formation of ketone bodies in that organ.

The facts that diabetes is more common in women than in men and that there are increases in incidence of the disease at puberty and at the menopause have suggested the existence of a relation between the sex hormones and the disease. A possible explanation of the high incidence at the menopause is the increase in pituitary activity which occurs at this period. There is an increase in the amount of follicle-stimulating hormone liberated, and it is postulated that there may also be an increased liberation of the diabetogenic hormone. Injections of estrin, which is known to depress the liberation of the follicle-stimulating hormone, cause a definite alleviation of the symptoms of diabetes and a decline in hyperglycemia and glycosuria. It is possible that the liberation of the diabetogenic hormone is also decreased by estrin, indicating an indirect relation of the sex hormones to diabetes through the pituitary.

Fasting women are more apt to develop ketosis than fasting men, a sex difference which is observed in several other species. Castration of the male does not affect the ketosis of fasting, although the removal of the sex glands from the female decreases ketosis to one quarter of its severity in the normal individual. Injections of anterior pituitary extracts into female castrates produce marked ketosis, although theelin injections have no such influence. These findings again suggest a reciprocal relation between the sex hormones and a pituitary hormone.

Removal of the adrenal glands causes a lowering of liver glycogen and a decrease in the ability of the animal to store glycogen. Anterior pituitary extracts which cause ketosis in normal animals have no such effect in adrenalectomized individuals. Removing both the pancreas and adrenals from animals and maintaining them on cortin enable them to survive three times longer than animals subjected to simple pancreatectomy. Facts such as these indicate the intimate relation between the adrenal cortex and the metabolic disturbances of diabetes.

Some diabetics have been observed to show a marked craving for salt, voluntarily ingesting as much as 80 grams a day. The administration of 1 or 2 grams of sodium chloride per kilogram each day has caused a decrease in the glycosuria of diabetics and an elevation of the respiratory quotient, provided that the potassium content of their basic diet was maintained at a low level. These findings are probably associated with the lowered sodium content of the blood serum and red cells, the lowered chloride of the serum and the elevated chloride of the cells associated with human diabetes. They are perhaps related to dysfunction of the adrenal cortex.

The pituitary is intimately connected with diabetes. Abnormalities of carbohydrate metabolism are frequently observed in pituitary dyscrasias, diabetic animals show hyperactivity of the pituitary, and ablation of the anterior pituitary increases the life span of depancreatized animals. Hypophysectomy in depancreatized animals lowers the blood sugar and, in some instances, curtails glycosuria; it causes a reduction in ketone-body formation and a return of the ability of the liver to store glycogen. Such animals are extremely sensitive to insulin, and injections of adrenalin produce only a very slight elevation of blood sugar. Liver glycogen may not be readily released, and there is a reduction in the rate of liver-glycogen formation. Several workers have postulated a pancreatropic hormone which they claim stimulates and causes an increase in the pancreatic islets.

The so-called diabetogenic hormone acts very rapidly, causing an increase in blood sugar and a decrease in liver glycogen. It possibly acts by way of the adrenal cortex, since its effects are not observed if the adrenals are ablated.

Injections of anterior pituitary extracts cause a disturbance in fat metabolism and an increase in ketone-body excretion. The principle causing these effects is different from the thyrotropic and diabetogenic fractions.

The parathyroid glands atrophy in depancreatized animals, and the plasma calcium falls to extremely low levels, while the phosphate is markedly elevated. The explanation of these observations is unsatisfactory, and further study with the aid of pure glandular extracts is necessary.

## FAULKNER HOSPITAL CLINICAL MEETING

The regular monthly clinical meeting was held at the Faulkner Hospital, Thursday afternoon, April 1.

The first case taken up for consideration was that of a young girl, 10 years of age, who had a rather typical picture of acute appendicitis. Unfortunately, 2 days had been allowed to elapse between the onset of abdominal pain and consultation with the surgeon. At operation an acutely inflamed appendix was found, which was removed, and a drain was left in. For 3 days following the operation the clinical chart looked satisfactory, but the patient remained distended with considerable discomfort and persistent vomiting. On the fourth day the tem-

perature, pulse and respirations began to rise somewhat. On this day, 2,000 cc. of fluid was given intravenously in divided doses of 1,000 cc. each. On the next day 1,000 cc. was given intravenously, and on the third day 1,000 cc. was given on two different occasions. Despite all treatment, the patient succumbed.

At autopsy the infection in the peritoneum showed evidences of healing. There were two small walled-off abscesses, one in the pelvis and one behind the cecum, which would probably have cleared up if the patient had survived. In the lungs there were an appreciable amount of bronchopneumonia and also pronounced edema. The heart showed dilatation of the right side in contrast to none on the left, but there was no evidence of myocardial degeneration.

The question which produced the most discussion was whether the dilatation of the right side of the heart, in contrast to the lack of dilatation on the left, and the pulmonary edema could have been due to the large amount of fluid which had been given intravenously in 3 days. Some of those present felt very strongly that this could happen. It is also rather distressing to realize that in these enlightened days a patient with appendicitis can be allowed to go 48 hours without surgical interference.

The other case was that of a man who had had a rather typical pneumonia without the type of the pneumococcus having been determined. A few days after his temperature had returned to normal, it again became elevated, and, at this time, it was found that there was a positive blood culture of the type I pneumococcus. Signs pointing toward the development of an endocarditis appeared, and the patient succumbed to a pneumococcus septicemia despite large amounts of type I antiserum. It was noted that, despite the previous pneumonia and the existence of a pneumococcus septicemia with type I pneumococci, there was no evidence of antibodies against this type of pneumococcus.

At autopsy, an acute valvular endocarditis due to the type I pneumococcus was present, in addition to pneumonia and empyema. The type I pneumococcus was found in the lungs, and it was also found in the empyema fluid. Microscopically the pneumococci were found deep down beneath the exudate and fibrin and in the connective tissue of the valve leaflet in a position where it would seem difficult for the antibodies of the antipneumococcus serum to penetrate. Whether the septicemia was a flare-up of the same organism that was present during the preceding pneumonia is not known, of course; but, in some cases, it has been reported that a subsequent septicemia was due to the same type of organism and, in others, to a different type from that which caused the pneumonia.

Dr. William R. Ohler, who presented the case, gave some statistics, which have recently been compiled from cases extending over a number of years, in regard to the percentage of mortality of pneumonia cases with positive blood cultures, grouped in accordance with the type of the pneumococcus. It was striking to learn of the high percentages of fatalities in cases with the type III pneumococcus. This organism, when pneumococci were first classified, was considered to be a very serious type. In subsequent years it did not seem to be so serious but apparently it causes fully as serious an infection as was originally feared, if the organisms are in the blood in sufficient numbers to give a positive blood culture. The results of the blood cultures in pneumonia cases are of considerable value from a prognostic point of view.

Due to illness, Dr. Calvin B. Faunce, Jr., was unable to give his talk on "Diagnosis and Treatment of Vertigo of Aural Origin," and Dr. Lyman G. Richards substituted.

The Faulkner Hospital has just been fortunate in receiving funds from one of its benefactors for the purchase of equipment for bronchoscopic work, and Dr. Richards spoke on "What Bronchoscopic and Esophagoscopic Examinations May Offer in Diagnosis and Treatment." In addition to presenting some interesting lantern slides, he emphasized the main symptoms for which these special types of examinations could be of benefit. In cases of hoarseness, unless the diagnosis can be cleared up by examination of the larynx with mirrors, an endoscopic study is indicated because treatment varies markedly, depending upon the cause of the hoarseness. In addition to the advantage of direct inspection for diagnostic purposes, a biopsy may be easily carried out through the endoscope. In respiratory obstruction, endoscopic investigation is frequently of value, because, although the x-ray may be helpful in the detection of foreign bodies, it must be remembered that some foreign bodies do not throw a shadow. On laryngeal narrowing, where intubation is indicated, direct examination of the larynx before insertion of the tube is frequently of value.

Dr. Richards showed a special instrument for intubation after direct examination. The introduction of a tube after endoscopic examination will often make a tracheotomy operation much simpler and more satisfactory.

He spoke of the success which has been obtained in some clinics from the drainage of chronic pulmonary suppuration through the bronchoscope but made it clear that by no means all cases of pulmonary suppuration could be benefited by this procedure.

He showed photographs of x-ray films, emphasizing the importance of taking x-ray films at the end of inspiration and at the end of expiration in order to demonstrate obstruction in the bronchi which results in emphysema on the affected side. These pictures were very striking because the side in which the bronchus was obstructed was not able to expel the air at the end of inspiration and showed a well-illuminated lung. He mentioned the fact that reports are beginning to appear about the beneficial effects of injections of lipiodol in cases of asthma. This was beside the subject for discussion, but it occurred to him when he was showing

some cases of bronchiectasis which had been diagnosed by lipiodol injections.

The symptoms which indicate the need for esophagoscopic examination are dysphagia and evidences of esophageal obstruction. As some of the causes of these symptoms can be favorably influenced by treatment, an exact diagnosis of the cause of the difficulty in swallowing or of the obstruction to the passage of food into the stomach is of importance. He also urged physicians to pay attention to the complaints of the patient and the story which the patient gives because, in his experience, it frequently happens that a patient has suggested repeatedly that it seemed as if there were a foreign body in the breathing apparatus or the swallowing tube, and yet the practicing physician has not given heed to the remarks of the patient.

## WILLIAM HARVEY SOCIETY

The monthly meeting of the William Harvey Society of Tufts College Medical School was held in the auditorium of the Beth Israel Hospital, Friday evening, March 5, Dr. Benjamin Sachs presiding. The subject, "Various Types of Grafts Used in Plastic Surgery about the Eyes," was discussed by Dr. John Martin Wheeler, professor of ophthalmology at Columbia University College of Physicians and Surgeons and director of the Eye Institute in New York.

Dr. Wheeler revealed that the subject had been suggested to him by his experience in three state medical board examinations when he was asked to describe the operation of skin grafting. Up to that time he had not realized the important part plastic surgery plays in the realm of medicine.

Plastic surgery was practiced as far back as early Egyptian times, but the most constructive work was done by the Italian, Gasparo Tagliacozzi, in the sixteenth century. He may rightly be called the father of this branch of medicine. He first attempted plastic repair of noses, lips and ears with good cosmetic results. Unfortunately, he also established the erroneous principle that all grafts must have a pedicle in order to live. This single axiom has markedly retarded the progress of plastic surgery even up to the present day.

In 1869, Reverdin demonstrated conclusively that all grafts need not have pedicles to be successful. He originated the principle of transplanting small islands of epithelium, introducing the punch grafts still widely used on large granulating surfaces.

Thiersch, in 1874, tried thin, razor grafts, and a few years later Wolff advocated the use of grafts of full skin thickness. Dr. Wheeler prefers the naming of grafts according to the layers of skin involved, such as dermal or dermo-epidermic, rather than by the classical historical nomenclature.

Plastic surgery may be defined as molding or sculptural surgery. Three main types of grafts may be used for this purpose: autoplastic, or grafts transferred from one part of an individual's body to another; homoplastic, or grafts moved from one to another of the same species; and heteroplastic, or transplants between different species. The latter two types are not successful, except with corneal transplants.

Pedicle grafts, although still used rather widely today with fair results, can be replaced in all but a few specialized cases by simpler and more adaptable methods. Since the major part of plastic surgery is done about the face, pedicle grafts usually involve the awkward fixation of relatively large portions or members of the body, such as the arms, for long periods. The more modern operations do not involve such disability. Pedicle grafts do, however, have a very definite value in those cases where the bed of the lesion is poorly vascularized, as in exposed bony surfaces. When used, they should be wider at the basal end than at the apex to prevent the loss of the apical portion because of insufficient nutrition. They may be used advantageously in repairing deficient eyelids. Dr. Wheeler demonstrated this application in a case of congenital absence of the upper lids with resulting blindness. Vision was recovered when pedicle grafts were advanced from the temporal regions to serve as functioning lids.

Dr. Wheeler pointed out that the disfiguring contractions of scars can be largely prevented if the healing process of the epithelium is clearly understood. Large granulating areas are prone to contract to a marked degree. If, however, epithelium such as the conjunctiva is used to cover areas which would otherwise granulate, the resulting contraction is insignificant. On convex surfaces, such as the scalp or cheek, contraction is not feared, but on concave surfaces even small scars may cause considerable distortion. In concavities, therefore, the entire surface of the graft must take. This is especially important in the region around the lower eyelid where the cosmetic results are so noticeable. Thin grafts with relatively little or no subcutaneous tissue diminish scarification. Another principle of great importance is the use of tissues that simulate the epithelium to be repaired as closely as possible. Dr. Wheeler demonstrated the point lucidly by citing one of his cases. The patient desired the removal of a birthmark involving a large area of the lower eyelid and cheek. The birthmark was excised. A graft from the upper lid was used for the surface approximating the lower lid. Postauricular grafts were employed for the cheek surfaces. In this way a remarkably good cosmetic effect was obtained.

The Reverdin or punch graft may be used successfully when convex surfaces, such as the upper eyelid, are involved. Even then, not all the islands of skin will take so that the use of this type of graft is usually confined to those cases where a functional success supersedes in importance the cosmetic effect, as in the wide destruction of tissue by a carcinoma. Another use of this method of grafting is in the repair of multiple, small, localized areas of skin damage, such as those which occur in powder burns from firearm accidents. The small areas of infiltration may be removed with a trephine.

This instrument is also used to remove the intended transplants from a suitable body surface. The punch grafts should fit as exactly as possible in order to obtain the best results.

For the purpose of filling cavity defects about the eyes, bone, cartilage or fascia may be used. Fascia, and in particular fascia lata, is by far the most adaptable tissue. Bone does not fit snugly, and cartilage is inclined to warp. Fascia can be accurately adjusted to the conformity and stays in place no matter what the type of cavity is or how much scar tissue lines it. If the underlying fascial filling is covered by a layer of epithelium to protect it from the air, it will live indefinitely. Fat has been used advantageously for cavity fillings and is especially useful in the orbit. It should only be used in relatively undamaged orbits for it has little supporting ability per se.

Bone grafts have only a limited use in the orbital region. They have been used with favorable results in cases of congenital absence of the roof of the orbit. Dr. Wheeler cited such a case where the defect caused a pulsation of the eyeball and paralytic squint, both of which symptoms were relieved by a bone graft from the outer table of the skull.

Full-thickness skin grafts of the type introduced by Wolff have a wide range of application in the plastic repair of the regions about the eye. Such grafts should include as little subcutaneous tissue as possible and are chiefly applied in cases of ectropion where they may be taken from the opposite uninjured lid or from elsewhere. In this type of repair it is well to remember that adequate support of the lower lid during the grafting period is absolutely essential. Such support may be accomplished by initiating the formation of small adhesions between the upper and lower lids by removing small approximating surfaces of lid margin. Adhesions will form between any two opposing injured epithelial surfaces. In this way the upper lid supports the lower for as long a period of time as is desired.

Corneal transplants are the only examples of successful homoplastic or heteroplastic grafts, excluding those of the very low-grade tissues. Eyes of stillborn infants, enucleated eyes and eyes of monkeys have been used with excellent results. Although vision is not always perfect, there is usually marked improvement. The avascularity of the cornea is probably an important factor in its advantageous use for grafting.

The replacement of eyelids and eyebrows presents a difficult problem to the plastic surgeon, because in transplanting large hair follicles a certain number of them will always die. The best results are obtained in grafts taken from analogous tissues, such as the opposite eyelid or brow. The scalp has been used with some success for the repair of eyebrows, but hair from this source is apt to grow indefinitely and irregularly.

Dr. Wheeler then took up the problem of artificial eyes. In this country the issue is an important one, while in Europe victims are content to wear patches. The lining epithelium of the socket should contain no hair follicles or sebaceous glands and should be inserted over a form which is held rigidly in place by a pressure dressing. The importance of this procedure cannot be overestimated, for it prevents hemorrhage and reduces granulation and, therefore, scarring.

Dr. Wheeler illustrated every important point of his interesting discussion with lantern slides.

## BOSTON SOCIETY OF ANESTHETISTS

The regular monthly meeting of the Boston Society of Anesthetists was held at the Hotel Kenmore on March 2. The following are abstracts of the talks given by Dr. Philip D. Woodbridge of Boston:

### METYCAINE SPINAL ANESTHESIA

Metycaine, a drug chemically related to procaine, has been used with satisfaction in over 1,500 spinal anesthesias. Its outstanding characteristic is that it produces anesthesia of 40 to 50 per cent greater duration than does procaine. Animal experiments have shown it to be of the same toxicity as procaine when given subcutaneously, and from two to four times as toxic when given intravenously. Clinically it has appeared to be no more toxic than procaine. Statistics were presented on 1,381 cases. The dose ranged from 40 to 200 mg., and a dose as large as 320 mg. was used in 1 case without deleterious effect. The technic of administration is similar to that of procaine. Anesthesia developed in from 3 to 8 minutes. In 90 per cent of the cases anesthesia was satisfactory, in 7.3 per cent fair, and in 2.7 per cent unsatisfactory. The common causes of dissatisfaction were retching and vomiting, insufficient length and insufficient height of anesthesia. In all cases in which operation was still going on at the end of 60 minutes spinal anesthesia was still present in 99 per cent, and at the end of 90 minutes in 73 per cent. As compared with procaine, the extra half hour of anesthesia which metycaine gives is of great advantage in such operations as cholecystectomy and combined perineal and pelvic operations. Anesthesia lasted at least as long as operation in 97 per cent of the cases. A statistical report of blood pressure changes during operation under metycaine showed it to compare not unfavorably with procaine in this respect.

There were no deaths attributable to spinal anesthesia. Postoperative shock occurred in 9 cases, and in 2 of these the anesthesia was thought to be a contributing factor. Troublesome postanesthetic headache occurred in 6 patients. In 5 of these it was relieved by shock position, and in no case was it persisting or extremely severe. Toe drop occurred in 6 cases. Two of these were not due to spinal anesthesia, 1 was probably due to spinal anesthesia or to psychoneurosis, and 3 appeared to be due to spinal anesthesia or to pressure from tight bedclothes immediately following operation. All cleared up within 6 months.

Metycaine is preferred to procaine for spinal anesthesia because of the greater duration of its effects without any apparent increase in toxicity. Pontocaine-glucose mixtures are very definitely preferred to both these drugs, however, because of the greater duration of anesthesia with considerably less depression of circulation and of respiration.

Metycaine is definitely preferred to procaine for local and regional anesthesia because anesthesia develops more promptly and surely, is more intense and lasts longer, solutions of metycaine keep for long periods without deterioration and are to some measure self-sterilizing, and the drug is effective when used by topical application in the eye or in the urethra.

### NUPERCAINE SPINAL ANESTHESIA

Nupercaine, a quinine derivative, is most frequently used in the form of Jones's preparation, a 1:1,500 dilution in 0.5 per cent saline solution. This solution is lighter than spinal fluid, is used in comparatively large volumes, and gives anesthesia of several hours' duration. It is particularly adapted to operations of unusual length and to those in which Trendelenburg position is wanted early. Eight cc. of the solution usually gives anesthesia of the lower extremities, 12 or 13 cc. of the lower abdomen, and from 16 to 20 cc. is used for the upper abdomen. A moving picture was shown of the technic of administration. Injection of the solution, warmed to body temperature, is made in the second lumbar space for abdominal anesthesia, the patient is placed in the prone position immediately following injection, and, if at the end of 4 minutes, anesthesia is not high enough, a bar is raised under the shoulders so as to make the region of the third or fourth cervical vertebra the highest portion of the spine, in order that the light solution may float upward toward this region. Anesthesia develops in from 4 to 12 minutes. The method is too cumbersome to be used for the majority of operations, but is very useful when unusually long anesthesia is desired. Relaxation has always been good, but the sensory effect is often not so deep as that obtained with procaine or metycaine. Depression of respiration and of circulation is relatively slight.

### REPORT OF CLINICAL TRIP

During a recent clinical trip the following miscellaneous items of practical interest were gleaned from various pharmacologists and anesthetists of the United States and Canada:

Spinal anesthesia for pulmonary lobectomy permits the patient to expectorate the large amounts of secretion which may give serious trouble under general anesthesia. The prone position is being used with satisfaction for thoracoplasty; its advantage is that it relieves the pressure on the good lung.

The danger of rupturing the lung by intratracheal insufflation of ether vapor has been overcome by resorting to a semi-open technic. The stem of a short T-tube is connected to the intratracheal catheter, one arm of the T-tube brings in the ether from the vaporizing apparatus, and the other arm of the tube is left open to the air.

The lateral decubitus position for patients immediately following operation successfully prevents inhalation of vomitus and obstruction of the airway.

Cocaine diminishes the vasopressor effects of ephedrine and of benzedrine but increases the effects of epinephrin, cobefrin, neosynephrin and epinine. Ergot and ergotamine lessen the vasoconstrictor effects of ephedrine and benzedrine and abolish that of epinephrin.

Circulatory collapse has been noted by a few anesthetists in occasional cases following cyclopropane anesthesia. It is not known whether this is caused by excessive amounts of carbon dioxide in the closed system, to inefficient action of soda-lime, to the sudden letdown to atmospheric concentration of oxygen from the high concentrations ordinarily used with cyclopropane, or to the toxic effects of the cyclopropane itself. Other anesthetists have not seen this postanesthetic effect.

Paraldehyde is probably a better and safer preliminary narcotic than avertin, and chloral hydrate a better anesthetic.

Barbiturates protect against anesthetic and surgical shock. Ether anesthesia causes an increase in blood lactic acid, sugar, phosphate, fat and rate of coagulation, an increase in protein metabolism, and a decrease in glycogen and alkali reserve, in blood volume and in bile flow. These changes are characteristic of shock, and are also produced by the administration of epinephrin. All these processes are eliminated or reduced by preliminary administration of barbiturates.

Excessive amounts of carbon dioxide are a likely cause of so-called "ether convulsions", for they seem most apt to occur when very tall semi-open masks are used to induce very deep anesthesia. Extreme concentrations of carbon dioxide may prevent the absorption of oxygen by hemoglobin, and thus bring about tissue anoxia even in the presence of high alveolar oxygen. In the presence of acidosis, with decreased carbon-dioxide combining power of the blood, a slight increase in alveolar carbon dioxide may precipitate convulsions without a preliminary state of hyperpnea. It is possible that many patients are killed by ill-advised carbon-dioxide therapy.

## CLINICAL MEETING OF THE STAFF OF THE MASSACHUSETTS GENERAL HOSPITAL

A clinical meeting of the staff of the Massachusetts General Hospital was held in the Moseley Memorial Building, March 11, Dr. Grantley W. Taylor presiding.

Two cases of gonococcal arthritis were presented, and the therapeutic measures applied to each were briefly discussed. Each patient had been subjected to several bouts of artificial fever, which was produced in one instance by injections of typhoid vaccine and in the other by use of the "hot box." Temperatures of 104° F. were maintained for from 4 to 12 hours. There was marked subjective and objective

improvement in both cases. Dr. Walter Bauer remarked that some 60 to 70 per cent of the cases of gonococcal arthritis could be cured by the use of good conservative treatment without resorting to fever therapy.

A case of syphilis of the central nervous system was presented. The patient had had a persistently positive spinal fluid serology with gold sol curves characteristic of tabes and paresis, in spite of the fact that there were never any clinical signs of syphilis of the central nervous system. A complete course of antisyphilitic therapy with arsphenamine and heavy metals and an intrathecal injection of arsphenamine had not produced any change in the spinal fluid reaction, so malarial fever therapy was instituted. The patient had already experienced seven of the ten paroxysms of fever, which are usually permitted, and it was stated that he was progressing satisfactorily. Dr. James B. Ayer stated that this form of treatment was being used much more commonly than in the past and expressed the belief that latent cases, such as the one described, should be so treated.

Dr. Stafford L. Warren, of the Strong Memorial Hospital, Rochester, New York, presented the paper of the evening on the subject "Recent Advances in Fever Therapy." Dr. Warren described physiologic studies of the effect of high-frequency currents. High-frequency currents follow the surface of the conducting material; and, therefore, the greatest current in the body is present in the skin, and the amount steadily decreases in the deeper tissues. The heating effect of these currents is due to the resistance offered by the tissues to the flow of the current, and the amount of heat liberated varies directly with the quantity of current flow. Therefore, the highest temperatures are obtained on the body surfaces, and relatively little heat is produced in the deeper body tissues. The circulating blood is of great importance in the production of artificial fevers, since it carries away and distributes throughout the body the heat liberated at the surface. The evaporation of sweat accounts for most of the heat lost from the body, and any interference with this process allows a rapid accumulation of heat, since it is possible to build heat up faster than it can be lost.

Radiant energy, as supplied by light bulbs in a cabinet, was found to be just as efficient as and much more inexpensive than the high frequency methods and is now used by Dr. Warren and his associates to produce artificial fever. Using this method, the body temperature is maintained at 106.7° F. for as long as 24 hours. It is considered unsafe to exceed this maximum temperature, since irreversible changes may occur in the cerebral cortex.

In the selection of patients to be submitted to fever therapy, a careful evaluation of the ability of the heart muscle to double its rate without undue fatigue or injury must be made. Careful supervision by a qualified physician must be maintained at all times during the treatment, and the cardiac rate and rhythm must be constantly followed for any signs of abnormality, which is considered as an indication for interruption of the treatment. Paraldehyde is administered intravenously or by rectum to prevent too great discomfort and violent delirium. Adequate fluid and salt balance must be established before beginning the treatment and must be carefully maintained throughout the fever.

Certain nonspecific mechanisms of resistance are temporarily enhanced by the fever treatment. The white count shows an elevation, and young polymorphonuclear leukocytes appear in the blood stream. The phagocytic powers of the blood are increased. Both of these phenomena fall rapidly after cessation of the fever.

Before a patient with gonococcal arthritis is subjected to fever therapy, the infecting strain of gonococcus is isolated, and its thermal death time determined by laboratory procedures. Temperatures above 39° C. are necessary to exert a good killing effect on gonococci, and the thermal death time is usually found to lie between 11 and 18 hours, with an average of 14 hours. It is the object of fever therapy to exceed this thermal death time in the patient's body, with hope that the infecting organisms will be destroyed. The defense mechanisms of the individual's body are of great importance in determining the outcome of the treatment. Better results are obtained with shorter treatments in patients with good resistance than are obtained with longer treatments in patients with a poor defense. Instances of failure of treatment have occurred in individuals with little resistance to the gonococcus and in cases in which the duration of fever was not great enough to exceed the thermal death time. There is no apparent correlation between the thermal death time and the duration, virulence or other manifestations of gonococcal infection.

Very satisfactory results were also obtained in the treatment of syphilis with artificial fever, a single prolonged fever often benefiting a paretic patient as much as chemotherapy. It is not believed, however, that primary and secondary syphilis can be cured by such treatment, since it is impossible to elevate the temperature of the cornea, head and respiratory passages to levels sufficiently high to kill the spirochetes which are present there.

The use of the fever cabinet and the technical procedures involved in the determination of the thermal death time of gonococci were illustrated with very excellent, colored motion pictures.

## NOTICES

### AMERICAN BOARD OF OPHTHALMOLOGY

The American Board of Ophthalmology has decided to establish a Preparatory Group of prospective candidates for its certificate, the plan being to assist physicians who wish to study ophthalmology so that they may become acceptable as candidates for examination and certification when they have completed the requirements.

Any graduate or undergraduate of an approved medical school is eligible to make application for membership in this group. Candidates so applying will be notified officially by the secretary when the Board has accepted their applications. If accepted, data will be sent concerning ethical and educational requirements. Syllabuses and other information will be made available to them.

Information and advice will be available to members in this group through preceptors who are members or associates of the Board. Members of the Preparatory Group must keep a summarized record of their activities, two copies of which will be sent to the secretary in January of each year and will be incorporated in the final application for examination and certification.

The fee for application for membership in the Preparatory Group will be $10. This will be deducted from the $50 which is required of every candidate for examination and certification.

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The American Board of Ophthalmology will conduct an examination in:

Chicago, October 9, 1937.

All applications and case reports, in duplicate, must be filed at least *sixty days* before the date of examination.

JOHN GREEN, M.D., *Secretary.*

3720 Washington Blvd.,
St. Louis, Mo.

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## NATIONAL HOSPITAL DAY

The member hospitals of the Massachusetts Hospital Association have all been asked to participate in the celebration of National Hospital Day, Wednesday, May 12. Stories about hospitals have been sent to the hospitals for newspaper releases in the various communities. The articles and the order in which they may appear throughout the state are as follows:

April 26. "Helping Folks to Get Well."
May 1. "The Hospital Goes to Picture Taking."
May 3. "About a Man Named Jones."
May 8. "Why I Chose a Hospital for My Birthplace."

Time "on the air" has been given to the committee by station WEEI for May 11 from 3:30 to 3:45 p. m. An effort is being made to have Governor Charles Hurley appear on this program.

Many of the hospitals in Massachusetts are planning to have open house for National Hospital Day, while others will conduct exhibits pertaining to hospital procedures. Teas will be given by nurses' alumnae and women's auxiliaries. Demonstrations by the medical staffs are on the programs of other hospitals.

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## MEDICAL CLINIC AT THE PETER BENT BRIGHAM HOSPITAL

At 3:30 p. m. on Thursday, April 29, in the amphitheater of the Peter Bent Brigham Hospital, Dr. Henry A. Christian, Hersey Professor of the Theory and Practice of Physic, Harvard Medical School and physician-in-chief, Peter Bent Brigham Hospital, will give a medical clinic. Practitioners and medical students are cordially invited to attend.

This will be the last clinic of the series. The next clinic will be on October 7.

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## CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

| Clinic Date | Orthopedic Consultant |
|---|---|
| Salem—May 3. | Dr. Harold C. Bean. |
| Haverhill—May 5. | Dr. Arthur T. Legg. |
| Lowell—May 7. | Dr. Albert H. Brewster. |
| Gardner—May 11. | Dr. Mark H. Rogers. |
| Brockton—May 13. | Dr. George W. Van Gorder. |
| Greenfield—May 14. | Dr. Harry R. Wheat. |
| Pittsfield—May 17. | Dr. Francis A. Slowick. |
| Springfield—May 19. | Dr. Garry deN. Hough, Jr. |
| Fall River—May 24. | Dr. Eugene A. McCarthy. |
| Hyannis—May 25. | Dr. Paul Norton. |
| Worcester—May 28. | Dr. John W. O'Meara. |

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## CORRECTION

In the notice of the death of Dr. Walter B. Bannerman, of East Bridgewater, which appeared in a recent issue of the *Journal*, it was erroneously stated that his son, Donald B. Bannerman, was a senior at the Boston University School of Medicine. The particular section should have read, "He is survived by . . . a son, Donald B. Bannerman, a senior at the Middlesex College of Medicine and Surgery. . . ."

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## HENRY JACKSON LECTURE

The annual Henry Jackson Lecture sponsored by the New England Heart Association will be held at the Boston Medical Library on Friday, April 30, at 4:45 p. m. The speaker will be Dr. Lewis A. Conner of New York. His subject will be "Comments upon Certain Aspects of Rheumatic Fever and Rheumatic Heart Disease." A short business meeting will precede the lecture. Physicians and students of medicine are cordially invited to attend.

JAMES M. FAULKNER, M.D., *Secretary.*

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## THE BOSTON MEDICAL HISTORY CLUB AND THE BOSTON MEDICAL LIBRARY

The Boston Medical History Club and the Boston Medical Library will hold a joint annual meeting Monday evening, April 26, at 8:15 o'clock, at the Boston Medical Library, 8 Fenway.

PROGRAM

"A Vesalian Miscellany." Archibald Malloch, M.D., Librarian, New York Academy of Medicine. Illustrated by lantern slides.

BENJAMIN SPECTOR, M.D., *Secretary.*

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## HOSPITAL COUNCIL OF BOSTON

The annual meeting of the Hospital Council of Boston will be held at the Hotel Puritan, 390 Commonwealth Avenue, Tuesday, April 27, at twelve-

thirty o'clock. Dr. Nathaniel W. Faxon will speak on "Plans for the Hospital Service Corporation." Doctors are cordially invited to attend. Luncheon $1. Reservations should be made with the Hospital Council of Boston, 80 Federal Street, by Saturday, April 24.

### BOSTON PATHOLOGICAL SOCIETY

The next meeting of the Boston Pathological Society will be held at Tufts College Medical School, April 30, at 8 p. m.

PROGRAM

1. The Relation of Chemical Allergy and Anaphylaxis. John L. Jacobs, M.D.
2. Neoplastic Changes of the Chorion. H. Edward MacMahon, M.D.

Physicians and medical students are cordially invited.

SIDNEY C. DALRYMPLE, *Secretary.*

### STAFF OF THE MASSACHUSETTS MEMORIAL HOSPITALS

The next meeting of the staff of the Massachusetts Memorial Hospitals will be held in the auditorium of the Evans Memorial, 78 East Concord Street, Friday evening, April 30, at 8:15 p. m.

PROGRAM

1. Report of a Case of Porphyria. Dr. B. S. Walker.
2. The Incidence and Course of Otitis Media in Scarlet Fever, as Influenced by Age, Mixed Infections, Season, Tonsillectomy, Paracentesis, Serotherapy and Prontylin. Dr. Conrad Wesselhoeft.

Discussion by Drs. E. H. Place, R. C. Eley, S. B. Hooker, H. L. Babcock, L. F. Johnson and E. C. Smith.

Physicians and medical students are cordially invited to attend.

HELMUTH ULRICH, M.D., *Chairman,*
LESTER R. WHITAKER, M.D., *Secretary.*

### ACADEMY OF PHYSICAL MEDICINE

The Academy of Physical Medicine will meet at Hotel Walton, Philadelphia, on October 19, 20, and 21, 1937. The secretary of the Academy is Herman A. Osgood, M.D., 144 Commonwealth Avenue, Boston.

### NEW ENGLAND SOCIETY OF PSYCHIATRY

The annual meeting of the New England Society of Psychiatry will be held at the Norwich State Hospital, Norwich, Connecticut, on Tuesday, April 27, at twelve noon.

The speaker will be Dr. Edward J. Humphreys, M.D., director of research, Letchworth Village, Thiells, New York, whose subject will be "Present-Day Research Trends in the Field of Human Deficiency."

HARLAN L. PAINE, M.D., *Secretary-Treasurer.*

### BOSTON UNIVERSITY MEDICAL SOCIETY

The next meeting of the Boston University Medical Society will be held in the Evans Memorial Auditorium, 78 East Concord Street, Boston, on Monday evening, April 26, at 8 o'clock.

PROGRAM

Presentation of Case.

Useful Hints in the Treatment of Gastrointestinal Disease. Dr. Walter C. Alvarez, Mayo Clinic, Rochester, Minn.

Medical students, nurses and physicians are cordially invited to attend.

ROBERT E. MOSS, *Secretary.*

### HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital amphitheater (Shattuck Street entrance), Tuesday evening, April 27, at 8:15 p. m.

PROGRAM

Presentation of Cases.

The Calcium Salts of Bone. Dr. Milan A. Logan.

Salt and Water Exchange between Tissues and Body Fluids. Dr. A. Baird Hastings, Department of Biological Chemistry, Harvard Medical School.

Medical students and physicians are cordially invited to attend.

MARSHALL N. FULTON, M.D., *Secretary.*

## SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, APRIL 26

**Monday, April 26—**

*8 p. m. Lecture on alcoholism, Dr. Timothy Leary, in the amphitheater of the Mallory Institute of Pathology, 784 Massachusetts Avenue, Boston.

*8 p. m. Boston University Medical Society. Evans Memorial Auditorium, 78 East Concord Street, Boston.

8:15 p. m. The Boston Medical History Club and the Boston Medical Library. Boston Medical Library, 8 Fenway.

**Tuesday, April 27—**

*9 a. m. - 10 a. m. Boston Dispensary, 25 Bennet Street, Boston. Recent Advances in Chemotherapy. Dr. A. Kenneth DeHart.

9:30 a. m. Massachusetts General Hospital. Thoracic clinic. Ether Dome.

*12:30 p. m. Hospital Council of Boston. Hotel Puritan. 390 Commonwealth Avenue, Boston.

*8:15 p. m. Harvard Medical Society. Peter Bent Brigham Hospital amphitheater (Shattuck Street entrance).

**Wednesday, April 28—**

8 a. m. Massachusetts General Hospital. Orthopedic grand rounds.

*9 a. m. - 10 a. m. Boston Dispensary, 25 Bennet Street, Boston. Hospital case presentation. Dr. S. J. Thannhauser.

†12 m. Clinicopathological conference. Children's Hospital amphitheater.

4 p. m. - 5 p. m. Surgical pathological conference. Dr. Cutler and Dr. Wolbach, Peter Bent Brigham Hospital.

**Thursday, April 29—**

*9 a. m. - 10 a. m. Boston Dispensary, 25 Bennet Street, Boston. Gastro-intestinal clinic. Dr. Katherine S. Andrews.

9 a. m. Massachusetts General Hospital. Surgical grand rounds.

9:15 a. m. Massachusetts General Hospital. Neurological conference.

12 m. Massachusetts General Hospital. Clinicopathological conference.
*3:30 p. m. Medical clinic at the Peter Bent Brigham Hospital. Dr. Henry A. Christian.

**Friday, April 30—**

*9 a. m. - 10 a. m. Boston Dispensary, 25 Bennet Street, Boston. Physical Conditions, Mental Health and Conduct. Dr. William Healy.
10 a. m. Massachusetts General Hospital. Fracture rounds.
12 m. Massachusetts General Hospital. Clinical meeting of the Staff of the Children's Medical Service. Ether Dome.
*4:45 p. m. Henry Jackson Lecture. Boston Medical Library, 8 Fenway.
*8 p. m. Boston Pathological Society. Tufts College Medical School.
*8:15 p. m. Staff of the Massachusetts Memorial Hospitals. Auditorium of the Evans Memorial, 78 East Concord Street, Boston.

**Saturday, May 1—**

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

*Open to the medical profession.
†Open to Fellows of the Massachusetts Medical Society.

**April 23**—Massachusetts Psychiatric Society. Page 678, issue of April 15.
**April 26**—Boston University Medical Society. Page 723.
**April 26**—The Boston Medical History Club and the Boston Medical Library. Page 722.
**April 27**—Harvard Medical Society. Page 723.
**April 27**—New England Society of Psychiatry. Page 723.
**April 27**—Hospital Council of Boston. Page 722.
**April 28**—New England Obstetrical and Gynecological Society. Page 633, issue of April 8.
**April 29**—Medical clinic at the Peter Bent Brigham Hospital. Page 722.
**April 30**—Henry Jackson Lecture. Page 722.
**April 30**—Boston Pathological Society. Page 723.
**April 30**—Staff of the Massachusetts Memorial Hospitals. Page 723.
**May 5**—George Washington Gay Lecture. Page 633, issue of April 8.
**May 5, 6, 7 and 8**—American Association on Mental Deficiency. Page 679, issue of April 15.
**May 7**—Boston Society for the Advancement of Gastroenterology. Page 678, issue of April 15.
**May 12**—National Hospital Day.
**May 13**—Pentucket Association of Physicians. Hotel Bartlett, 95 Main Street, Haverhill, at 8:30 p. m.
**June 7**—American Medical Golfers Play in Atlantic City. Page 582, issue of April 1.
**June 7-11**—American Medical Association. Atlantic City. Page 709.
**June 8**—The American Neisserian Medical Society. Page 489, issue of March 18.
**June 8 and 9**—American Board of Obstetrics and Gynecology. Page 78, issue of January 14.
**June 11-18**—Catholic Hospital Association. Page 488, issue of March 18.
**July 6-11**—Fifth International Congress of Hospitals. Page 37, issue of January 7.
**September 13-17**—Fifth International Congress of Radiology. Page 709.
**October 5-8**—American Public Health Association meeting. New York City.
**October 9**—American Board of Ophthalmology, Chicago. Page 722.
**October 19, 20, 21**—Academy of Physical Medicine. Page 723.
**October 25-29**—American College of Surgeons. Chicago, Illinois.

## DISTRICT MEDICAL SOCIETIES

### ESSEX SOUTH DISTRICT MEDICAL SOCIETY

**May 12**—Annual meeting. Salem Country Club. Speaker: Dr. P. P. Johnson of Beverly. Subject: A Trip to the Bahamas and Guatemala. (Illustrated.)

R. E. STONE, M.D., Secretary.
74 Lothrop Street, Beverly.

### FRANKLIN DISTRICT MEDICAL SOCIETY

Will meet at the Weldon in Greenfield at 11 a. m. the second Tuesday of May.

CHARLES MOLINE, M.D., Secretary.
Sunderland.

### HAMPDEN DISTRICT MEDICAL SOCIETY

**April 27**—Hotel Kimball, Springfield. 4:15 p. m.
**May 6**—Censors' meeting. 20 Maple Street, Springfield. 4 p. m.

### MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

**May 12**—Bear Hill Golf Club, Stoneham.

KENNETH L. MACLACHLAN, M.D., Secretary.
1 Bellevue Avenue, Melrose.

### NORFOLK DISTRICT MEDICAL SOCIETY

**May**—Annual meeting. Details to be announced.
**May 6**—Censors' meeting.

FRANK S. CRUICKSHANK, M.D., Secretary.
1247 Beacon Street, Brookline.

### PLYMOUTH DISTRICT MEDICAL SOCIETY

**May 20**—11 a. m. Lakeville State Sanatorium.

FRED F. WEINER, M.D., Secretary.
231 Main Street, Brockton.

### SUFFOLK DISTRICT MEDICAL SOCIETY

**April 28**—Annual meeting. Boston Medical Library, 8:15 p. m. "Problems in Surgical Diagnosis." Dr. Howard M. Clute.

CONRAD WESSELHOEFT, M.D., President,
CHARLES C. LUND, M.D., Secretary.

### WORCESTER DISTRICT MEDICAL SOCIETY

**May 6**—At 4:30 in the rooms of the Worcester Medical Library, Inc., at 34 Elm Street, Worcester, will be held the spring meeting of the Board of Censors.
**Wednesday Afternoon and Evening, May 12**—Annual meeting.

ERWIN C. MILLER, M.D., Secretary.
27 Elm Street, Worcester.

### WORCESTER NORTH DISTRICT MEDICAL SOCIETY

**April 28**—Meeting will be held at the Burbank Hospital, Fitchburg, at 1 p. m.

## BOOKS RECEIVED FOR REVIEW

**Clinical Roentgenology of the Cardiovascular System.** Hugo Roesler. 343 pp. Springfield and Baltimore: Charles C Thomas, 1937. $7.50.

**Transactions of the American Association of Genito-Urinary Surgeons.** Forty-Eighth Annual Meeting held at Stockbridge, Massachusetts, May 25, 26 and 27, 1936. Volume XXIX. 502 pp. Saint Paul and Minneapolis: The Bruce Publishing Company, 1936.

**Preoperative and Postoperative Treatment.** Robert L. Mason. 495 pp. Philadelphia and London: W. B. Saunders Company, 1937.

**The Diseases of Infants and Children.** J. P. Crozer Griffith and A. Graeme Mitchell. Second Edition, Revised and Reset. 1154 pp. Philadelphia and London: W. B. Saunders Company, 1937. $10.00.

**Children Handicapped by Cerebral Palsy.** Psychological Factors in Management. Elizabeth Evans Lord. A Medical Explanation by Bronson Crothers. 105 pp. New York: The Commonwealth Fund, 1937. $1.25.

**Aids to Pathology.** Harry Campbell and Kenneth Campbell. Seventh Edition. 263 pp. London: Baillière, Tindall & Cox, 1936. $1.50.

**Aids to Diagnosis and Treatment of Diseases of Children.** F. M. B. Allen. Seventh Edition. 329 pp. London: Baillière, Tindall & Cox, 1937. $1.50.

**Modern Discoveries in Medical Psychology.** Clifford Allen. 280 pp. London: Macmillan Co., Ltd., 1937. $2.75.

**Clinical Laboratory Diagnosis.** Samuel A. Levinson and Robert P. MacFate. 877 pp. Philadelphia: Lea & Febiger, 1937. $9.50.

**A Handbook on Diseases of Children Including Dietetics, Welfare and the Common Fevers.** Bruce

Williamson. Second Edition. 329 pp. Baltimore: William Wood & Co., 1936. $4.00.

**An Introduction to General Practice.** E. Kaye Le Fleming. 150 pp. Baltimore: William Wood & Co., 1936. $2.00.

**The Operations of Surgery.** R. P. Rowlands and Philip Turner. Eighth Edition. Volume II, the Abdomen. 998 pp. Baltimore: William Wood & Co., 1937. $10.00.

**The Chemistry of Natural Products Related to Phenanthrene.** An American Chemical Society Monograph. L. F. Fieser. Second Edition. 456 pp. New York: Reinhold Publishing Corporation, 1937. $7.00.

**Medical Greek and Latin at a Glance.** Walter R. Agard. Second Edition, Revised. 87 pp. New York: Paul B. Hoeber, Inc., 1937. $1.50.

**Temple University Obstetrical Guide-Book.** J. O. Arnold. 197 pp. Philadelphia: Corson Publishing Company, 1937. $2.50.

**Internal Diseases of the Eye and Atlas of Ophthalmoscopy.** Manuel Uribe Troncoso. 530 pp. Philadelphia: F. A. Davis Company, 1937. $15.00.

**Safe Childbirth: The Three Essentials.** 1. Round Brim. 2. Flexible Joints. 3. Natural Posture. Kathleen Olga Vaughan. 154 pp. Baltimore: William Wood & Co., 1937. $3.00.

**Cancer and Diet.** With Facts and Observations on Related Subjects. Frederick L. Hoffman. 767 pp. Baltimore: The Williams & Wilkins Company, 1937. $5.00.

**Senile Cataract.** Methods of Operating. W. A. Fisher. Third Revised Edition. 150 pp. Chicago: The H. G. Adair Printing Co., 1937. $2.00.

**Ophthalmoscopy, Retinoscopy and Refraction.** With New Chapter on Orthoptics. W. A. Fisher. Fourth Revised Edition. 210 pp. Chicago: The H. G. Adair Printing Co., 1937. $2.00.

## BOOK REVIEWS

**Oral Diagnosis and Treatment Planning.** A Textbook for Students and Practitioners of Dentistry and Medicine. Samuel Charles Miller. 620 pp. Philadelphia: P. Blakiston's Son & Co.

This book represents an effort on the part of twenty-two contributors, each an authority in a special field, to give the dental student the means of improving his diagnostic ability and of correlating various phases of medical and dental problems in the oral cavity.

It is a comprehensive volume of more than six hundred pages and is divided into twenty-six chapters, which are profusely illustrated. The first chapter is a general outline of the signs of oral diagnosis, supplemented by specific charts for the student to follow. The second and third chapters deal with head pains and pains of dental origin. They are well written in a practical and instructive manner.

The other chapters cover the entire field of dentistry and oral surgery. As is the case with most books compiled by various writers, this book contains repetitions and lacks a certain amount of continuity among the various chapters. However, the editor has tried to minimize this defect by skilful arrangement of the chapters.

It is probably the first time that dental literature has brought forth such an extensive work on the diagnosis of dental diseases. It is valuable not only for students and practitioners of dentistry, but also for physicians. There are chapters of interest to the latter, especially those that cover the diseases of the oral mucous membranes, mouth infections and their relation to systemic disease, oral and dental diseases of occupational origin and oral manifestations of endocrine dysfunction.

**Surgery for Dental Students.** Philip H. Mitchiner, Clement E. Shattock, Edward G. Slesinger, and Cecil P. G. Wakeley. 364 pp. Baltimore: William Wood & Company. $4.75.

This book, as stated by the authors, has been written to provide the dental student and practitioner with a work to which he can refer for practical guidance regarding the care of surgical conditions. The material is divided into nineteen chapters, of which the first deals with general surgical pathology. The succeeding chapters describe major surgical operations for such conditions as wounds, tumors, surgical diseases of the blood vessels, nerves, lymphatics, fractures, and so on, and the book ends with a discussion of the nose and eyes.

The authors have laid special emphasis on surgical diseases in which the dental student has direct interest, such as diseases of the mouth, teeth and jaws. Their approach is in simple and concise language, supplemented by instructive illustrations. In the hands of the dental student, the book would serve as a useful syllabus on surgery and surgical pathology; from it he can gather a good deal of knowledge, which can be amplified, if desired, by consultation with more exhaustive texts.

**The Harvey Lectures.** Delivered under the Auspices of The Harvey Society of New York. 1935-1936. Series XXXI. 255 pp. Baltimore: The Williams & Wilkins Company. $4.00.

As usual, this annual lecture series covers a wide field. The titles give the scope of the volume: "Proteins and Proteolytic Enzymes," by Dr. Max Bergmann; "The Significance of Chimpanzee-Culture for Biological Research," by Prof. Robert M. Yerkes; "The Virus Tumors and the Tumor Problem," by Dr. Peyton Rous; "Relations between the Parathyroids, the Hypophysis and the Pancreas," by Dr. B. A. Houssay; "The Interrelation of Cerebrum and Cerebellum in the Regulation of Somatic and Autonomic Functions," by Dr. John Farquhar Fulton; "The Influenzas of Swine and Man," by Dr. Richard E. Shope; "Malignant Cells," by Dr. Warren H. Lewis, and "The Physiology of the Bronchial Vascular System," by Dr. I. de Burgh Daly. All of the lectures are of high quality and give, in concrete form,

the substance of advance research by men eminent in various aspects of scientific endeavor. They cannot be abstracted for review as they are already condensation of thought and epitomes of biologic studies. Their various appeal should be welcome reading for those working in the same or allied subjects, although the charm of the individual presentation is lost in the printed page.

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**The Legal Aspects of Milk Control.** James A. Tobey. 102 pp. Chicago: International Association of Milk Dealers.

The history of the legal aspects of milk control forms an important and well-nigh fundamental chapter in the public health history of the country. The ability to control milk supplies through legislation by the several states lies in their police power, one of the rights specifically reserved to the states under the Constitution. The gradual development of the legislative control of milk is an excellent illustration of the way in which the police power of the states has been applied for promoting the welfare of the people. Valuable precedents for public health legislation have been established through court decisions on various aspects of the legal control of milk supplies.

Consequently Dr. Tobey, in collecting and compiling this monograph on the development of milk control legislation, has made a worthwhile contribution to the history of public health measures in the United States. The subject matter is succinctly treated in ten chapters, covering the reasons for public control of milk; sanitary regulation of milk by the state; municipal control of milk; licenses and permits; standards for milk and dairy products; inspection, sanitation and seizure of milk; tuberculin testing and the health of dairy cattle; pasteurization; containers for milk; and liability in connection with dairy products. There is an excellent bibliography of cases, a table of cases by states and a bibliography. The work constitutes a valuable textbook for health officers, students of public health and those engaged in the production and sale of milk.

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**Physical Diagnosis.** Ralph H. Major. 457 pp. Philadelphia and London: W. B. Saunders Company. $5.00.

Major's textbook of physical diagnosis is of an ideal size. The illustrations are unsurpassed. The introductory chapters on the history of physical diagnosis and on pain are of much interest and value. The work as a whole is easy to read. But the reviewer cannot agree that extrasystoles and auricular fibrillation "may be diagnosed by simple inspection of the carotid pulse without palpating the radial pulse or listening to the heart." One may well take exception to the statement that syphilis is a cause of aortic stenosis. The descriptions of vesicular and bronchial breathing, although of historical interest, do not, in the reviewer's opinion, convey a very clear idea of the characteristics of their sounds. It is unfortunate that in this, the first edition, the pulmonary artery is depicted as arising from the right auricle. Cardiac irregularities, surely an important subject, are but briefly discussed. Similarly, chronic pulmonary tuberculosis is too summarily dismissed. There is a certain amount of unnecessary repetition especially in relation to heart murmurs. It may well be questioned whether respiration is slowed "in obstructions to the bronchus." One searches in vain for a clear description of the signs and symptoms of cardiac failure.

On the whole, the reviewer cannot recommend this book to students of the subject.

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**Rural Health Practice.** Harry S. Mustard. 603 pp. New York: The Commonwealth Fund. $4.00.

This author is now associate professor of public health administration in the School of Hygiene and Public Health of Johns Hopkins University. Although such positions sometimes imply a relatively sheltered life, such cannot have been the case in this instance.

The book is a text of nearly six hundred pages, none of which have strayed very far from the title. Rural health practice is defined; its historical background is cited; its varied forms and promotion are discussed; and its responsibilities are placed in a very readable and satisfactory manner. Anyone who has interested himself in local public health problems to the extent of entering the inevitable petty conflicts which arise will find much to vindicate his hurt and possibly repressed feelings. Although political chicanery, outmoded personnel and other such rancors are dealt with barehanded, there is no righteousness in the author's style. His discussions of finances, budgets, salaries and selection of quarters all indicate that they are written by a man who has been there.

Among many excellent chapters, one on epidemiological considerations stands out particularly. The reviewer even read the chapter on syphilis, which calls for exceptional fortitude nowadays.

Altogether it is a well-conceived, well-written and well-printed work; the first to appear in its special field, and one which will become an indispensable help to all who hope to practice modern public health in a rural community. The reviewer makes this prediction with considerable confidence.

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**Research in Dementia Precox.** [Sic.] Nolan D. C. Lewis. 320 pp. New York: The National Committee for Mental Hygiene. $1.50.

This monograph which is a publication of the research project directed by the National Committee for Mental Hygiene and financed by the Scottish Rite Masons is an extensive bibliography and digest of books and articles published. Presumably the product of several workers, it is valuable as a reference compilation. It disappoints the reader, however, insofar as critique or originality is expected.